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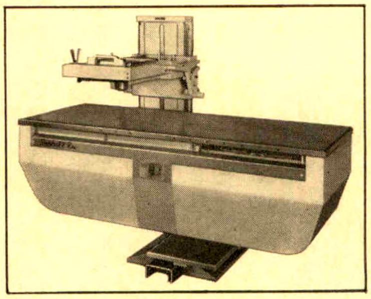

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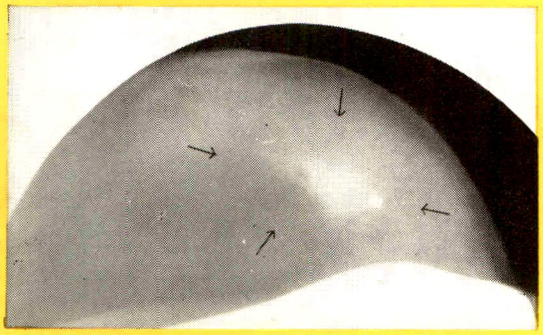
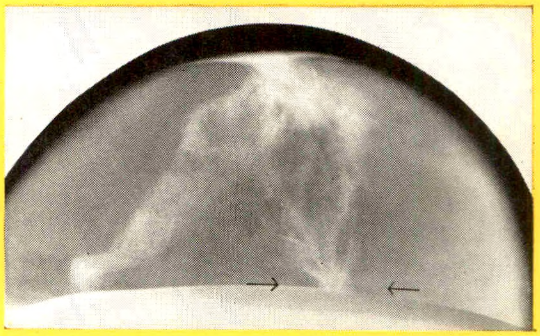


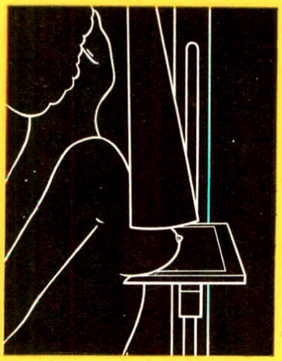
Woman of 74. Clinical examination revealed mastitis with carcinoma a possibility. X-ray confirmed the carcinoma.

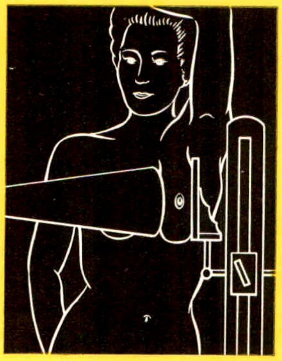


Woman of 69. Clinical examination revealed only a retracted left nipple. X-ray revealed a small carcinoma.

Typical Positioning Procedure

A cranio-caudal view is taken with the patient sitting. The breast rests on the film, which is carried on a small lead covered table, adjustable in the vertical plane. Cones used for this technique are equipped with a perspex plate over the mouth to provide necessary compression.





For a lateral view, the patient normally stands with hand on head. The cone is turned into the horizontal position and the film is fixed in the vertical plane. Again, the breast is compressed against the film by the specially equipped cone.

Material excerpted from "X-Ray Focus," Vol. 5, No. 1, published by Ilford Limited, London

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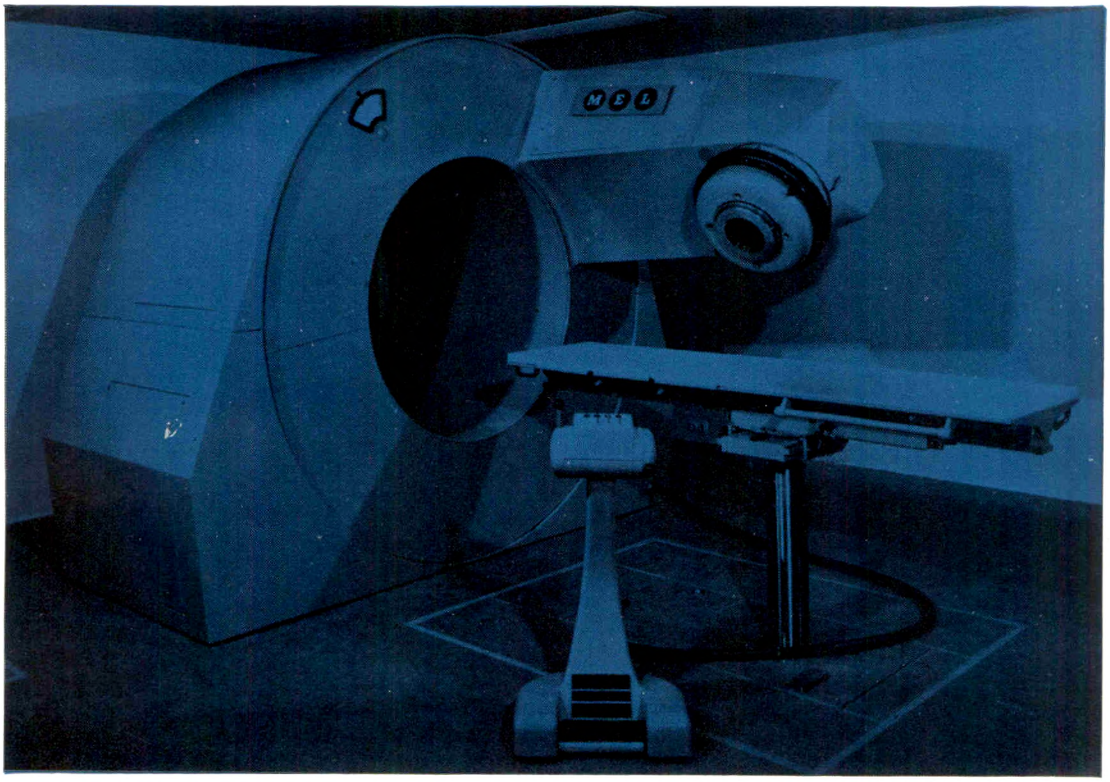

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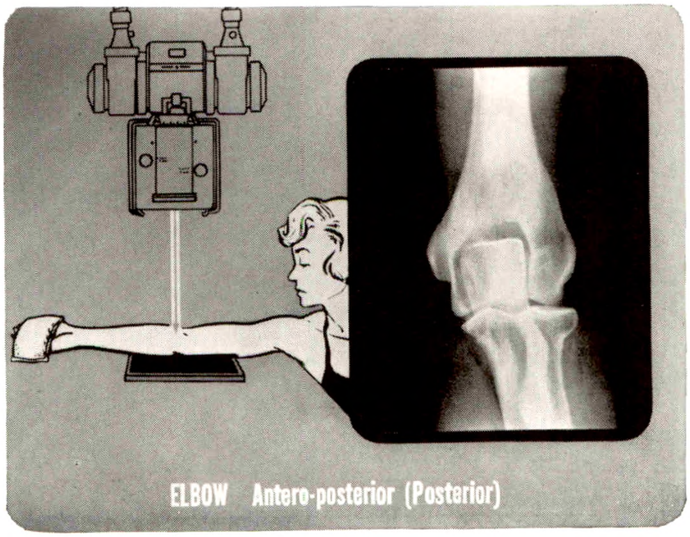

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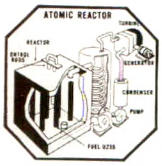

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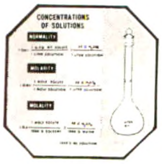

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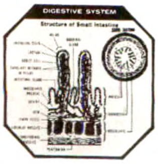

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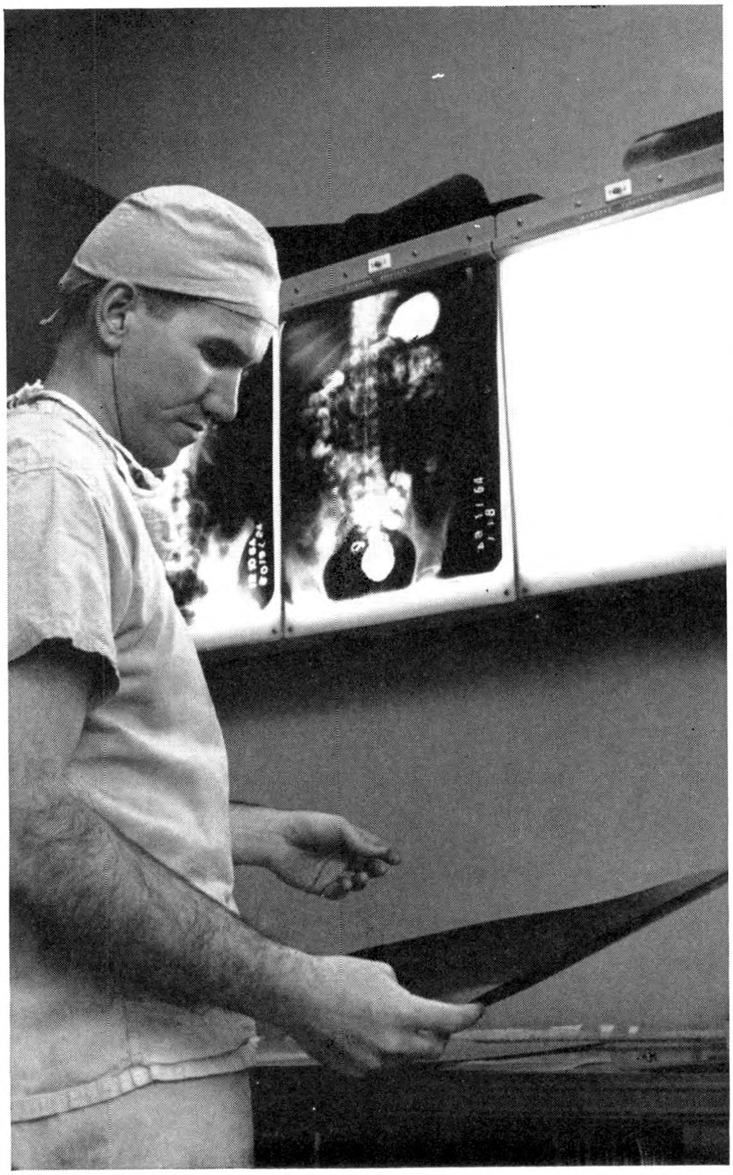

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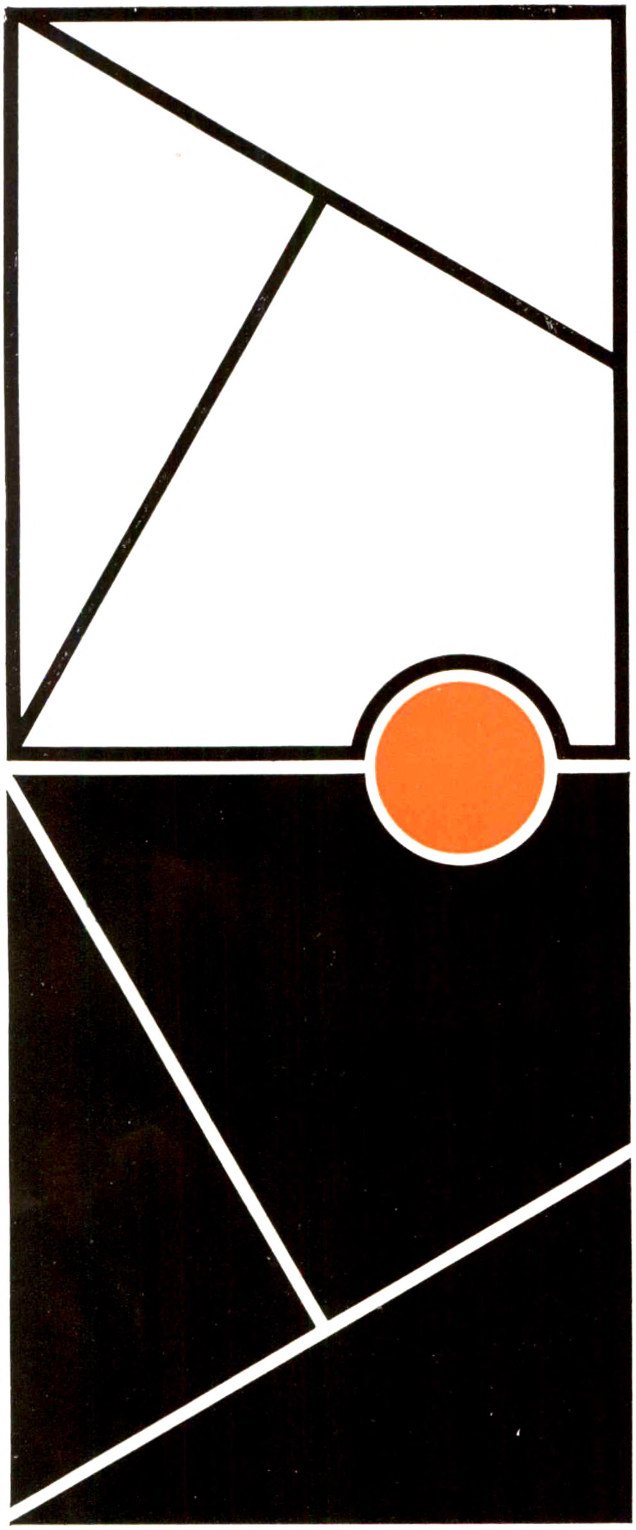

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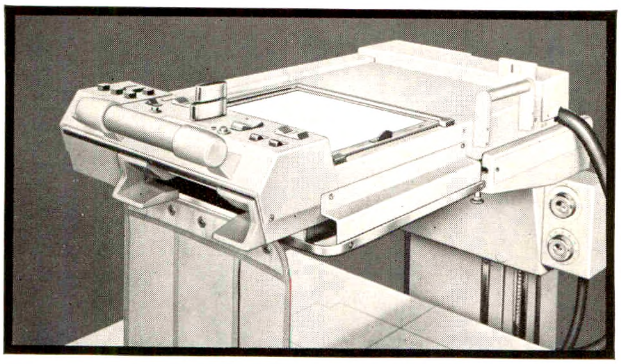

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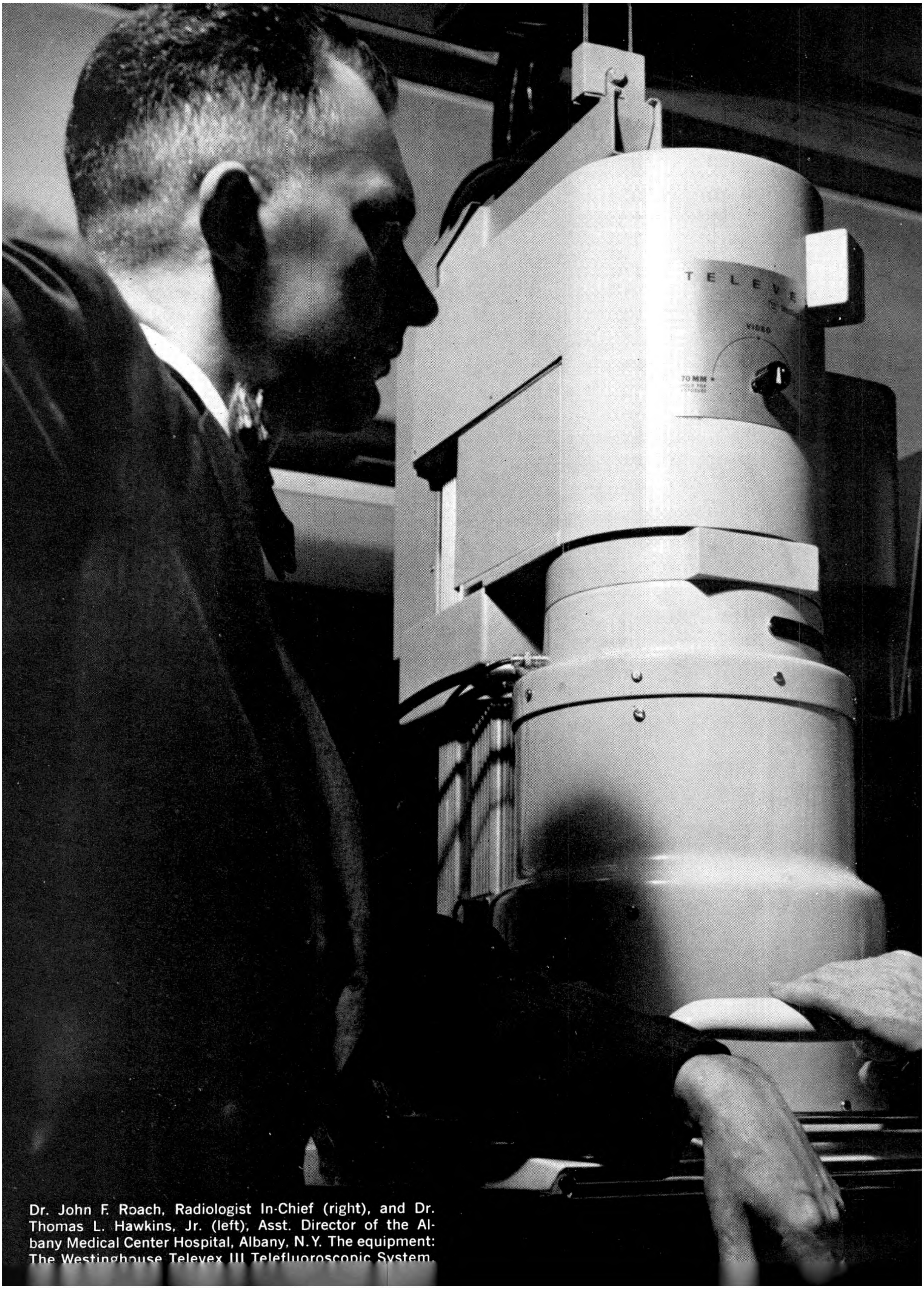

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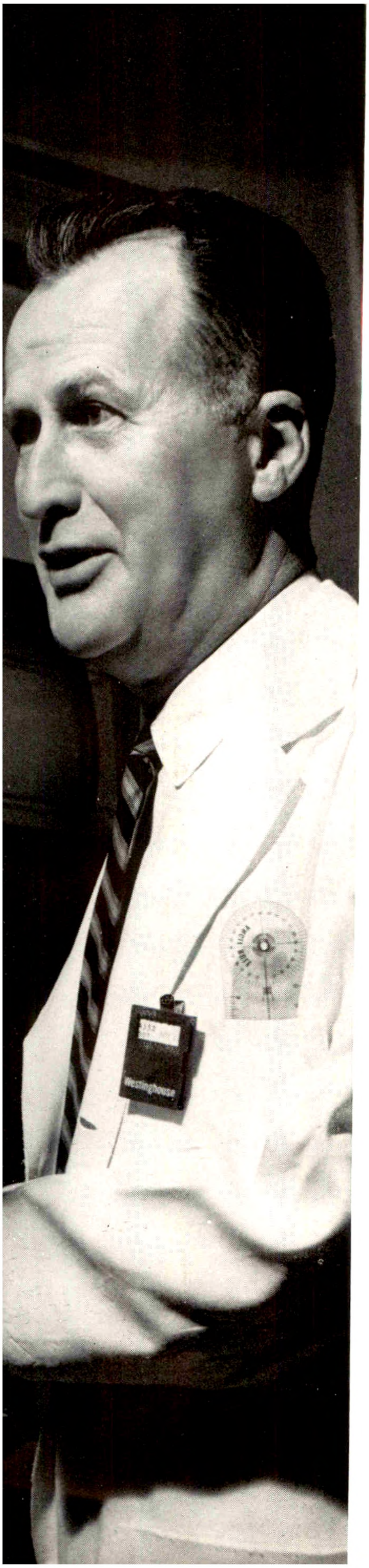

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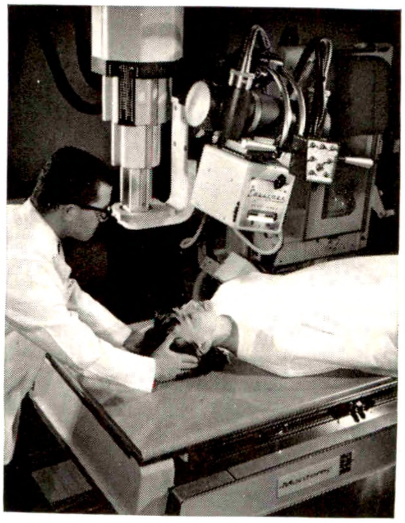

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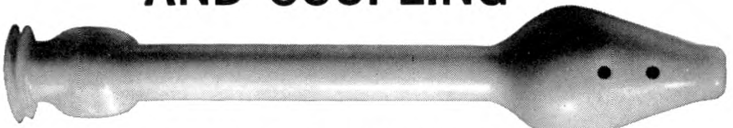

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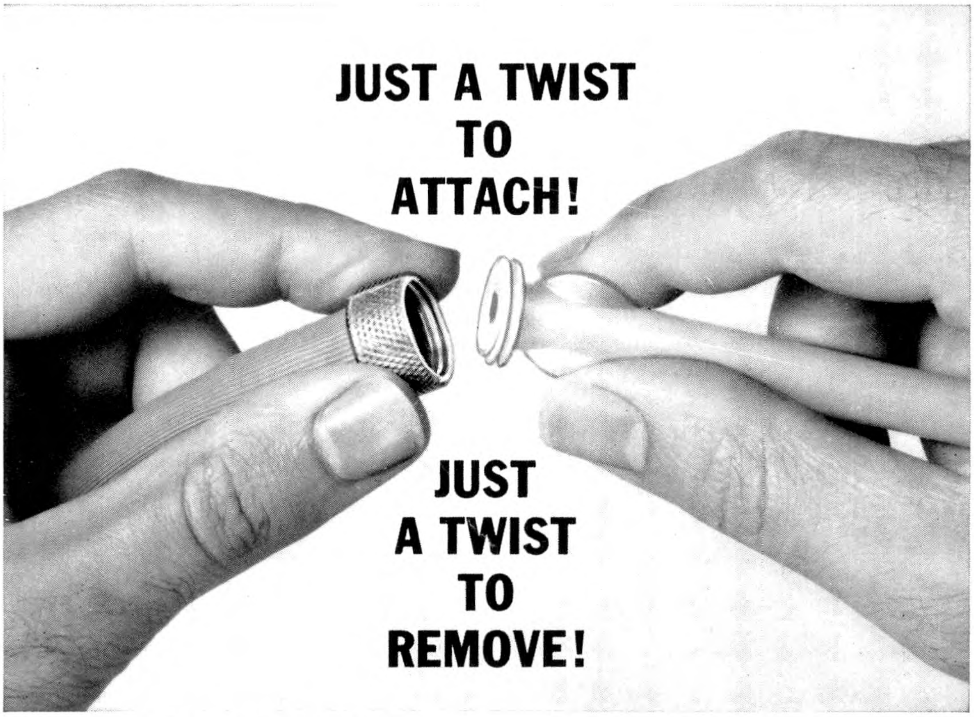

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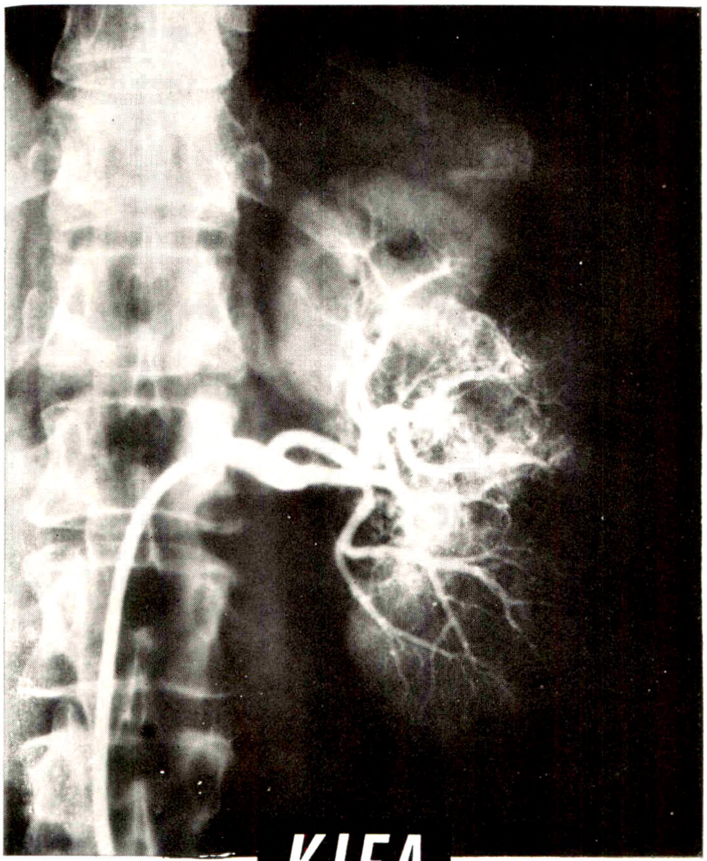

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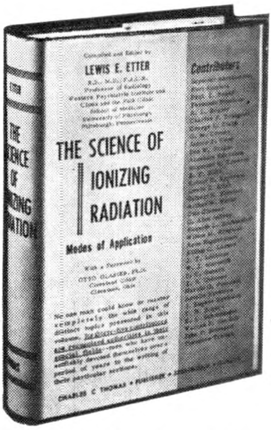

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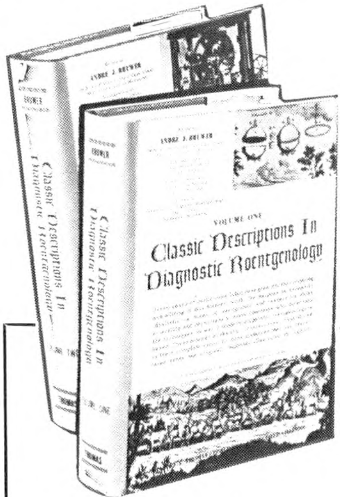

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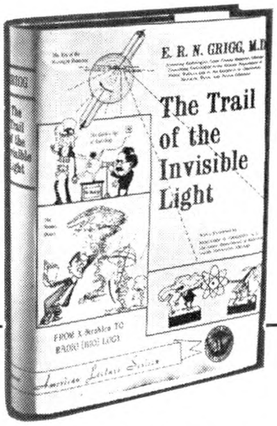
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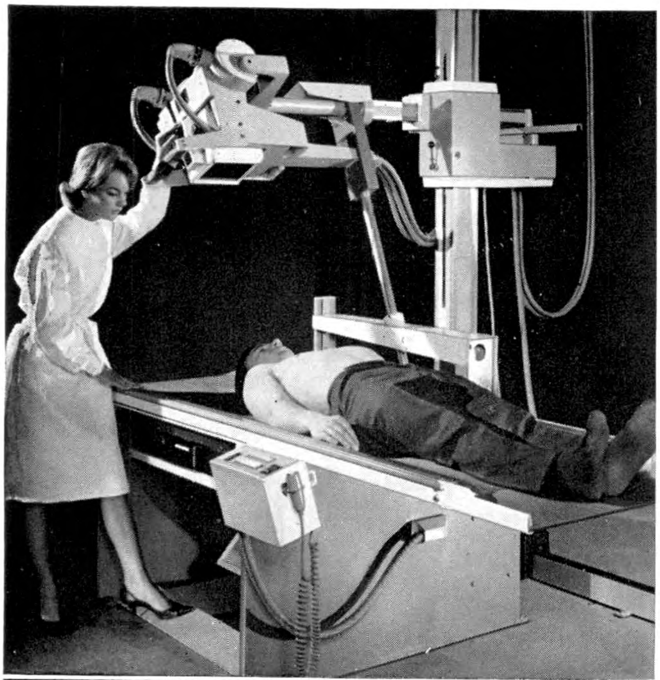

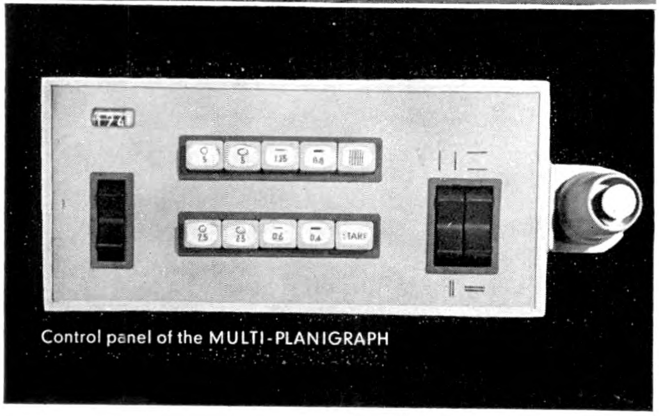

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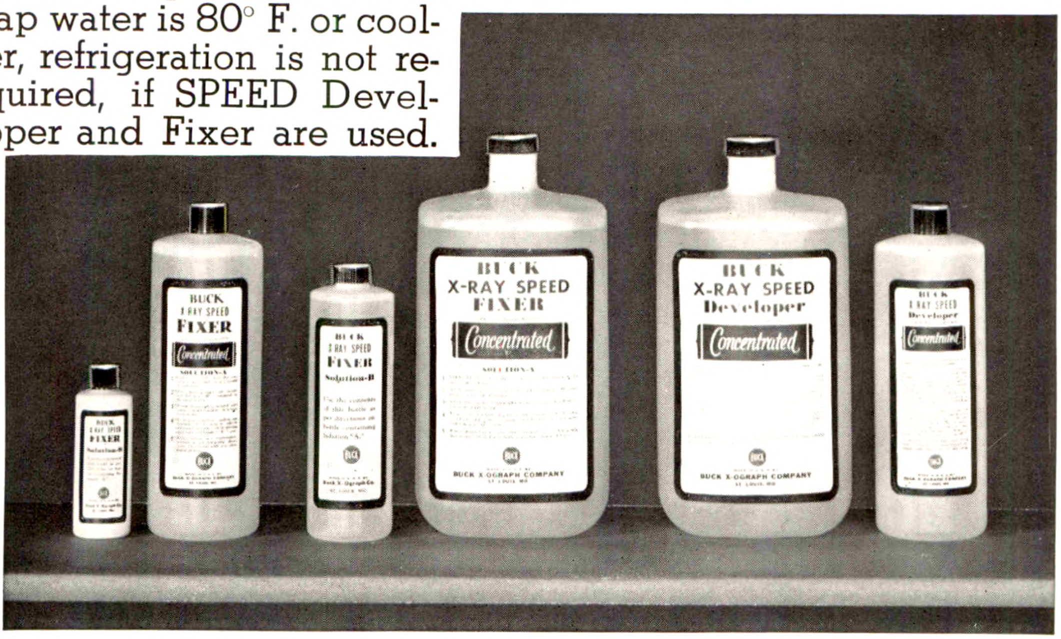

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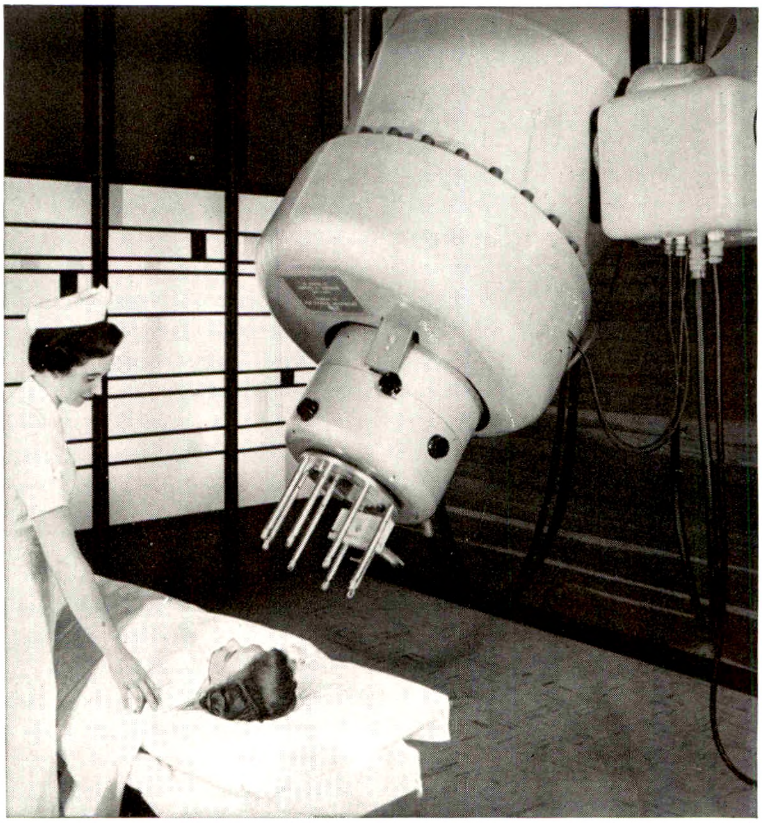

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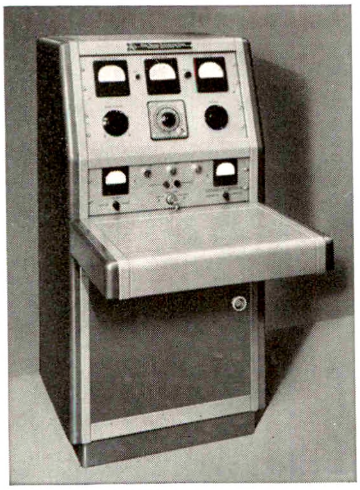

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RADIOIODINE AND THE CHILD WITH THYROID CANCER*

By FREDERICK J. BONTE, M.D.
DALLAS, TEXAS

ALTHOUGH cancer arising in the thyroid gland is not an especially common neoplasm, circumstance has often made it a well publicized one. Because many thyroid carcinomas and their metastases retain the parent-cell property of trapping and binding iodine, these were among the first cancers to lend themselves to both diagnosis and treatment by the new techniques of the atomic age. Later, thyroid neoplasia became a battleground for proponents of various liberal and conservative methods of diagnosis and treatment around which a surprisingly large literature has accumulated, not only in medical journals but in the popular press. Currently, the problem of cancer and the solitary thyroid nodule is receiving wide attention. From these many controversies, one can select a few common points of agreement: as with other thyroid diseases, cancer affects the female more often than the male; in recent years the incidence of thyroid cancer seems to be increasing in young persons; the average patient who is found with this disease may expect to survive it.

ETIOLOGY

The etiology of thyroid neoplasia has been studied intensively. Thyroiditis, developmental and iodine-deficiency goiters, and pre-existing thyroid adenomas have all been designated as premalignant lesions,[15,21] but none can be fully established in this role. Recent interest, however, has centered upon the effects of exposure of the thyroid gland to ionizing radiation. In the years since 1950, when an etiologic relationship between radiation and thyroid cancer was first proposed by Duffy and Fitzgerald,[5] the radiation histories of large numbers of patients with thyroid neoplasms have been analyzed, and, likewise, information has been gathered about the occurrence of thyroid disease in large groups of people who have histories of suitable radiation exposure. The fine review article of Root[21] will furnish a good background on these

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Table I

HISTOLOGIC CLASSIFICATION OF 468 OF THE 704 CASES WHICH COMPRISE THE CHILDHOOD THYROID CANCER REGISTRY*

Papillary carcinoma	74%
Follicular carcinoma	18%
Undifferentiated cancer	8%

* Winship, T., and Rosvoll, R. V.[28,29]

studies. One central theme may be derived from these efforts: whether or not the data from all available series will withstand all of the statistical tests which may be applied to them, common sense suggests a causal relationship between exposure of the neck to relatively large amounts of ionizing radiation and the development of thyroid cancer.

From the United States and from world experience, Winship and Rosvoll[28,29] have collected 704 cases which form the Childhood Thyroid Cancer Registry. Detailed histories have been obtained for 366 of these children. Eighty per cent of them had a history of exposure of the thyroid region to doses of ionizing radiation in the range of 120 to 6,000 rads at some time during early infancy or childhood. The most common reason seemed to be the accidental inclusion of the thyroid gland in unnecessarily large ports directed at the thymus. There is a good deal of geographic variation which, of course, is dependent upon the popularity of thymus irradiation in a given area, and the care with which certain radiotherapists limited exposure to the upper mediastinum. The thyroid was also, on occasion, incidentally exposed during the treatment of tuberculous cervical lymphadenitis and the reduction of superabundant lymphoid tisue.

As opposed to the relatively frequent association of cancer and irradiation in children, it is far less common to elicit a significant history of radiation exposure during adult life from a patient who has developed thyroid cancer.[20]

In childhood the phenomenon of induction of neoplasia in the thyroid gland by ionizing radiation behaves as if it were a threshold process with the threshold dose of the order of 100 to 150 rads, but at about the time of puberty the threshold dose seems to become a good deal higher. It is interesting to note the relatively high incidence of thyroid neoplasia in the thyroid glands of young children who were exposed to ionizing radiation either from external beam or radioisotope sources.[21,26] On the other hand, there is little reason to suspect increased thyroid neoplasia in the group of some 200,000 individuals who have been treated during adulthood for benign thyroid disease with radioiodine. In fact, there is as yet no authenticated report of the development of a thyroid malignancy in an adult as a consequence of radioiodine therapy. The difference may be explainable on the basis of the fact that the growing thyroid gland in childhood is relatively hyperplastic, and, in the experimental animal at least, pre-existing hyperplasia is a necessary condition for the induction of neoplasia by ionizing radiation.

It seems fair to state that although ionizing radiation seems to be a contributing cause in the development of cancer of the thyroid gland in some individuals, it is by no means the sole etiologic factor in this disease.

HISTOLOGIC CLASSIFICATION

All of the various histologic types of thyroid cancer which occur in adults are to be found in children, but fortunately with a slightly higher proportion of differentiated carcinomas. Table I shows the classification of 468 cases from the Childhood Thyroid Cancer Registry.[28] Ninety-two per cent were differentiated carcinomas representing 74 per cent papillary carcinomas and 18 per cent follicular adenocarcinomas. The remaining 8 per cent were such undifferentiated cancers as the small and giant cell carcinomas, the Hürthle and spindle cell cancers, and the interesting, amyloid-containing medullary carcinomas of relatively good prognosis.

Papillary carcinomas often contain follicular elements, and pathologists may describe these as mixed papillary and follicular adenocarcinomas. In most localities these are the most common of thyroid malignant tumors. Follicular elements may predominate in their metastases, and both tumors and their metastatic extensions may behave in a markedly thyroid-like manner, incorporating iodine and elaborating thyroid hormone.

DIAGNOSIS

Children of any age may be found to have thyroid cancer, and malignant thyroid tumors have even been reported in newborn infants and in very young babies.[14] Principal clinical danger signals include persistent or progressive cervical or supraclavicular lymphadenopathy and the presence of thyroid nodules. The discovery of a multinodular goiter in a child is always an indication for its surgical removal, since from 40 to 60 per cent of such goiters will be found to contain cancer. Solitary nodules, too, will represent cancer oftener in children than in adults. Lymphadenopathy is the most common manifestation of childhood thyroid cancer, however, for lymph node metastases are present in about three-fourths of all children at the time of diagnosis.[29]

The physical examination of any child who has cervical lymphadenopathy should include a thorough palpation of the thyroid gland, but, as in adults, the primary lesion may be quite small, and so the diagnosis of thyroid cancer in children is usually made by lymph node biopsy. The concepts of "benign metastasizing struma" and "lateral aberrant thyroid" are no longer held at most institutions, and the presence of thyroid tissue in lymph nodes of the neck is regarded as evidence of metastasis from a thyroid adenocarcinoma.

When a thyroid cancer has been identified in a child, additional diagnostic tests which are obtained should include roentgenograms of the chest, skull and axial skeleton, and scintillation scans or directional counts of suspected metastases, employing one of the radioactive isotopes of iodine. Well-differentiated thyroid carcinoma in a child may function vigorously in the presence of considerable normal thyroid tissue and may incorporate a goodly amount of radioiodine—an occurrence sometimes observed in adults as well.[7] Not only does this assist in the diagnosis of otherwise unsuspected tumor deposits, but it introduces the possibility of radioisotope therapy. The decision whether or not to use isotopes for treatment in a given case of thyroid cancer is based in part on the amount of tracer retained in tumor tissue, which may be measured by direct counting, or inferred from a 48 hour urinary excretion test (Table v). This test and the method of its application will be described in more detail in a later section of this paper.

TREATMENT AND PROGNOSIS

The principal figure in the initial management of thyroid cancer should be a surgeon trained and skilled in thyroid cancer surgery. He must design an operation appropriate to the extent of the disease and to the condition of a particular patient. Under extreme circumstances he may merely be able to establish a satisfactory airway, but ideally he will perform a thyroidectomy in such a way as to spare only one or two thyroid remnants about the parathyroid glands. Segmental thyroidectomy and thyroid lobectomy are no longer regarded as satisfactory operations for the removal of even the most highly differentiated of carcinomas. The work of Rose *et al.*[23] supplies ample evidence in support of bilateral lobectomy, for they have shown a 35 per cent incidence of tumor in spared thyroid lobes.

Routine radical lymphadenectomy is seldom performed for thyroid cancer, but a lymph node dissection of some scope is usually attempted. With low-grade tumors special scintillation detectors may be introduced into the surgical field, and the operation may consist of the removal of tracer-containing tissue.

TABLE II

CHILDHOOD THYROID CANCER REGISTRY
DEATHS FROM THYROID CANCER*

Mortality = 115/704	Per Cent = 14.9
59% died within 5 years	
18% died between 5 and 10 years	
23% died after 10 years	

* Sixty-eight per cent of those who died of thyroid cancer had differentiated tumors.[28,29]

SELECTION OF FURTHER TREATMENT

If there is reason to believe that the primary tumor has been completely removed and no metastases can be demonstrated in lymph nodes or in distant parts of the body, no additional treatment is given. Prophylactic ablation of thyroid gland remnants with radioactive iodine is not usually carried out either in adults or in children. Such patients should be followed carefully clinically, with roentgenographic studies, and in the Radioisotope Laboratory for local recurrence or distant spread of the disease.

UNDIFFERENTIATED CARCINOMA

If the cancer is found to be one of the various undifferentiated neoplasms, postoperative external beam therapy must be employed in children as it is in adults, for there is no other hope for survival if there is residual primary tumor. Some of the entities in this group, such as small cell carcinoma, are quite radiosensitive, but all seem potentially radiocurable to some degree, however slight. Perhaps a third of all undifferentiated cancers might be controlled by this sort of management.

DIFFERENTIATED CARCINOMA

In adults, postoperative external beam radiotherapy is sometimes used to attempt control of residual differentiated tumor in the primary site, and it is regularly employed against soft tissue and osseous metastases, especially those which will not respond to radioisotope treatment. Radioiodine is used freely in adults for destruction or extended control of suitable thyroid carcinoma, but it is used carefully, according to patient exposure rules which have been dictated by accumulated experience.[1,9,10,12,16,19,22,27]

The situation with respect to postoperative radiotherapy in children who have well-differentiated carcinoma must be examined at some length; however, the most important factor to be considered in selecting appropriate treatment is the natural history of the disease itself. The course of the average low-grade tumor is of such duration that many misunderstandings have developed about the nature of these cancers. One will occasionally still encounter physicians who believe that differentiated thyroid carcinoma is not a fatal disease; nothing could be further from the truth.

MORTALITY

The mortality of thyroid cancer in childhood matches that for adults, as is shown by the statistics of the Childhood Thyroid Cancer Registry in Table II. Not only did 15 per cent of these children die from their disease, but two-thirds of those who died had well-differentiated carcinoma.[28]

On further study of Table II, we find that only 59 per cent of the children who died of thyroid cancer did so within 5 years of diagnosis. Forty-one per cent died 5 years or more after the discovery of disease, and of these, 23 per cent died after 10 years. More than half of all mortality is caused by local extension to vital structures in the neck and the remainder by metastasis and dissemination.[28]

It is easy to see how misunderstandings may arise about the lethality of a neoplasm with these characteristics. It is also clear that the usual 5 year period of observation is not nearly long enough. A child who has been treated for thyroid cancer probably should be seen in follow-up for the rest of his life.

MODE OF TREATMENT

On the other hand, while differentiated thyroid carcinoma may on occasion be a mortal disease, cure or extended control is obviously to be anticipated in from 80 to 90 per cent of any group of affected children,[9,10,16,27,29] and even those who are living with disease may do so for many years. Therefore, the initial treatment given the child with a well-differentiated neoplasm must be designed to preserve certain important functions. For example, sacrifice of the recurrent laryngeal nerve is no longer considered justified in the surgical approach to such a tumor,[18] nor is radical thyroid-parathyroidectomy practiced at this time. If conservative surgical procedures are done, circumstances are bound to arise in which cancer must be left in the primary site, or in surgically inaccessible locations in the neck, or in a distant part of the body. There may even be a postoperative recurrence.

When there is no further resort to surgery, some form of radiotherapy must be employed, for the only alternative therapeutic possibility, suppression of tumor growth by the administration of large doses of thyroid hormone, has been proven to be ineffective[22,29] and it should never be employed as a primary method of treatment of inoperable thyroid tumor.

Some differentiated cancers cannot be made to accept significant amounts of radioiodine, and external beam radiotherapy is the only adjunctive treatment available for this disease, but the low-grade tumor of childhood may concentrate enough isotope to make this treatment modality feasible. In a child, the decision between external beam and radioiodine therapy is a difficult one to make, for there are disadvantages inherent in each of these methods.

POSSIBLE SEQUELAE AND HAZARDS OF IRRADIATION

In a small neck, the necessity of incorporating osseous growth centers in the volume irradiated by an external beam technique means the likely production of kyphoscoliotic deformities of the cervical spine and possible subsequent neurologic disabilities. Further, heavy irradiation of the cervical spinal cord must certainly be avoided in a child who may well survive his disease.

There has even been speculation about the possibility of laryngeal hypoplasia and chondromalacia resulting from irradiation of the larynx of a very young child. This remains only a theoretic hazard, however, for it cannot be proved or disproved by the scant available literature. The only reported instances of laryngeal damage by ionizing radiation in children with consequent hypoplasia or atrophy are in a group of 4 cases described by Clerf[4] in 1927, in which the doses of radiation delivered by intralaryngeal radium application were not measured, but presumably were huge. No complication of this sort is known to Winship,[28] nor has Schweisguth,[24] of the Gustave-Roussy Institute, who collects similar material from European centers, any record of such an occurrence.

Radioisotope irradiation of iodine-concentrating tumor deposits is an intriguing form of radiotherapy, for, while theoretically sparing adjacent normal tissues, one can deliver a much higher tumor dose than with external beam techniques, perhaps by a factor of two or three to one. The method is certainly not without its drawbacks, for whole-body radiation is delivered by the circulating and diffusing radioiodine at an average ratio of about 0.5 to 1.5 rads per mc given by mouth, depending upon the size of the child (Table VI). Under extreme circumstances serious effects have even been exerted upon surroundng normal tissue, as in the case of the radiation fibrosis of lung which has been known to follow repeated radioiodine treatment of pulmonary metastases.[19] The administration of doses of radioiodine in the curie range has been known to produce radiation nephritis, but these are no longer used.

Minor complications include the transient sterility[11] and hypoparathyroidism which have resulted on very rare occasions. The major cause of concern in using radioiodine, however, is the irradiation of the whole body in general and of the hematopoietic system in particular, and the possible development of radiation-induced leukemia.

In an experience in which large doses of the order of hundreds of rads were given to the marrow of the axial skeleton in the course of treatment of rheumatoid spondylitis with external beam techniques,[8] it is easy to relate irradiation to the induction of leukemia. With the much smaller doses of whole-body radiation, such as those delivered by radioiodine administered for the treatment of benign thyroid disease, probably in the range of 1 to 30 rads, the incidence of acute leukemia may or may not differ from that to be expected in the general population. Whole-body radiation from therapeutic doses of I^{131} which one might give to children might lie in a range between these two experiences, perhaps 10 to 50 rads, and one cannot predict with any assurance whether such doses will produce leukemia or not. The individual child who may be treated with radioiodine for thyroid adenocarcinoma can be expected to be at risk for a relatively long time after radiation exposure, tending to increase the hazard. While it is reassuring to learn that there has been no reported case of leukemia arising within the group of just over 100 patients in the Childhood Thyroid Cancer Registry[28] who have received one or more treatment doses of radioactive iodine, it scarcely need be said that the group is too small and the average period of observation too short for firm conclusions to be drawn. Perhaps a review of some representative cases and the problems they presented might help in the formulation of a general approach to the child with thyroid cancer, and might define the circumstances in which radioiodine might be employed.

CLINICAL FEATURES

The records of Parkland Memorial Hospital show that but 78 cases of thyroid cancer have been seen in the Clinics and in the Radioisotope Laboratory during the past 20 years, 64 of them since the formation of the present Department of Radiology in July, 1956. In general, these cases show the usual sex and race distribution, and the small group is notable only for the number of young people it contains. In 11 of these patients, thyroid cancer was discovered during or before the 15th year of age, and in 12 more the diagnosis was made from the 16th to the 26th year. Since many of the patients were referred for study from other institutions it would not be safe to draw any conclusions about an increasing incidence of juvenile thyroid carcinoma on the basis of this one experience. It is interesting to note that there is very little background of significant exposure to therapeutic radiation, for there is no history of exposure in the group of children 15 and under, and only 2 of the 12 young adults from 16 to 26 years of age give such a history. A complete analysis of the older patients has not been undertaken.

PATIENT MATERIAL

The 11 patients in whom the diagnosis was made during or before the 15th year were considered to have developed cancer in childhood. Table III is a summary of pertinent information on these cases: we shall review a few more fully.

UNDIFFERENTIATED CARCINOMA

In the childhood thyroid cancer group there was but 1 case of undifferentiated carcinoma.

Patient 1 was a 15 year old boy who was brought into the emergency room at Parkland Memorial Hospital on October 9, 1950, semiconscious and breathing laboriously. A firm, rubbery 6×5 cm. mass was present in the thyroid region and was fixed to surrounding soft tissues. Enlarged lymph nodes were palpable at the periphery of the primary tumor mass bilaterally. Anxious relatives provided only a sketchy history of a rapidly growing mass which had appeared recently, perhaps within the past few weeks. Preliminary attempts to

Table III

ELEVEN CASES OF THYROID CANCER OCCURRING IN CHILDREN, AGE 15 YEARS AND YOUNGER, SEEN AT PARKLAND MEMORIAL HOSPITAL*

Patient	Age at Diagnosis	Race	Sex	Presenting Sign	Pathologic Diagnosis	Local Extension	Metastases	Treatment		Present Status
								Surgery	Irradiation	
I	15	N	M	Thyroid mass	Small cell carcinoma	Invasion of trachea and muscles	Regional lymph nodes	Thyroidectomy 10-9-50		Died 10-9-50
II	13	W	F	Thyroid nodule	Papillary and follicular adenocarcinoma	None	Regional lymph nodes	Thyroidectomy and right neck dissection 10-20-61		No evidence of disease
III	12	W	M	Enlarged neck lymph nodes	Papillary carcinoma	None	Regional lymph nodes	Thyroidectomy 2-8-62 and 2-14-62		No evidence of disease
IV	12	W	F	Enlarged neck lymph nodes	Papillary and follicular adenocarcinoma	None	Regional lymph nodes	Thyroidectomy 1-15-64; neck dissection 2-23-63		No evidence of disease
V	9	W	M	Enlarged neck lymph nodes	Papillary and follicular adenocarcinoma	Invasion of trachea, esophagus, muscle	Regional lymph nodes	Thyroidectomy 10-17-60	I^{131} 22.9 mc 11-22-60	No evidence of disease
VI	5	W	F	Thyroid mass	Papillary and follicular adenocarcinoma	Invasion of Muscle	Regional lymph nodes	Thyroidectomy 1-9-57 recurrence March, 1960; recurrence Jan., 1961; recurrence Aug., 1961	Roentgen rays Jan., 1958 3,500 r; I^{131} 25 mc 11-13-61	No evidence of disease
VII	10	W	F	Neck lymph nodes	Papillary and follicular adenocarcinoma	Invasion of thyroid cartilage, muscle, trachea	Regional lymph nodes; posterior cervical lymph nodes	Exploratory operation 12-1-60; thyroidectomy 12-14-60	I^{131} 50 mc 2-24-61	No evidence of disease
VIII	15	N	F	Thyroid mass	Papillary and follicular adenocarcinoma	None	Regional lymph nodes by scan only	Thyroidectomy 7-18-56 and 7-26-56	I^{131} 100 mc 8-12-58	No evidence of disease
IX	14	N	F	Enlarged neck lymph nodes	Papillary and follicular adenocarcinoma	None	Regional lymph nodes	Thyroidectomy 4-13-55 and 4-27-55	Roentgen rays primary tumor May, 1955, 4,000 r; I^{131} 100 mc 10-8-57	No evidence of disease
X	14	W	M	Enlarged neck lymph nodes	Papillary carcinoma	None	Regional lymph nodes 1943; lungs 1950	Thyroidectomy 1940, 1943; Lymph node biopsy 1950	Roentgen rays primary tumor 1943, 3,000 r? I^{131} 552 mc 1950-1962	Living with lung metastases
XI	15	N	F	Thyroid nodule	Papillary and follicular adenocarcinoma	Pericapsular	Regional lymph nodes June, 1958; lungs by scan only Dec., 1959	Thyroidectomy 3-15-56	Roentgen rays primary tumor April, 1956, 3,500 r; I^{131} 100 mc 7-2-58; I^{131} 85 mc 12-30-59	No evidence of disease

* History of exposure of the neck to ionizing radiation is negative for Patients II through XI. No radiation history is available for Patient I.

establish an airway were not entirely successful, and the patient was prepared for surgery on an emergency basis. Local decompression of a highly aggressive, invasive tumor was performed, and a tracheostomy tube was inserted. Despite these measures the patient died 4 hours after the conclusion of the operation, with the exact cause of death not clearly defined. Tissue presented for pathologic examination was identified as small cell carcinoma of the thyroid gland. This is a rare neoplasm in children, and it apparently pursues the rapid and morbid course often observed in adults. The tumor is a radiosensitive one, and potentially radiocurable.

DIFFERENTIATED CARCINOMA

The remainder of the children had differentiated carcinomas, 8 identified as mixed papillary and follicular adenocarcinomas and the other 2 as papillary carcinomas. Nine out of 10 had evidence of extension of thyroid cancer beyond the primary site at the time of initial operation.

No Residual Tumor. In 3 patients who had regional lymph node metastases, all disease has apparently been controlled by the initial surgical procedure, at least during our relatively short period of observation. The following case is illustrative:

Patient 11 was a 13 year old girl who was found to have a soft nodule in the thyroid gland in July, 1961, when examined because of pharyngitis. By October, the nodule had increased significantly in size, for it was now a firm mass which measured about 2 cm. in diameter and occupied the superior pole of the right thyroid lobe. On October 20, 1961, a thyroidectomy was done, sparing parathyroid tissue in the left upper pole area. During the operation enlarged lymph nodes were found along the right internal jugular chain, and frozen section histologic examination yielded a diagnosis of well-differentiated papillary and follicular adenocarcinoma. A right cervical lymphadenectomy was performed, but the left cervical region was not approached. Of 8 large lymph nodes removed, 5 were found to contain tumor. The patient recovered satisfactorily from the operation, but a question arose about the nature of the lymph nodes palpable in the left cervical area. She was referred to the Radioisotope Laboratory for additional follow-up on June 4, 1962.

When we first saw the patient, she appeared to be in good general condition. A few small, soft lymph nodes were palpable along the lateral margin of the left sternocleidomastoid muscle and at the left mandibular angle. Thyroid replacement with 2 grains of thyroid extract daily had been instituted in January, 1962. Chest and skeletal roentgenograms were obtained and showed no evidence of metastases, and a 25 μc tracer of I^{131} as sodium iodide was given orally. This resulted in the accumulation of a very small amount of activity, and so an additional 100 μc tracer dose was given, together with an intramuscular injection of 10 units of thyroid stimulating hormone (TSH).* The only activity which could now be found in the neck by directional counting and scintillation scanning was at the site of thyroid tissue surrounding the spared parathyroid gland on the left side. No further treatment seemed to be in order at that time.

Since then the patient has been seen at intervals of about 3 months. From time to time lymph nodes have been found to be enlarged during upper respiratory infections, but the lymphadenopathy had subsided by the time of the next examination. At 2 of the 4 yearly visits, small tracer doses of I^{131} were given with TSH and directional counts were made over the thyroid region and various areas of the neck, with special attention being directed to lymph nodes which might at that time be palpable. At no time has there been evidence of metastasis in the form of significant lymphadenopathy, nor has periodic roentgen examination disclosed any. There will be no need for treatment until active disease is discovered. We will continue to see the patient at 3 month intervals as long as she is available for follow-up. Tracer tests will be done on an annual basis from now on, and replacement thyroid hormone level will require occasional adjustment.

Comment. It was not thought necessary to ablate the remaining normal thyroid gland, for there was no evidence of the presence of metastatic tumor. Unnecessary whole-body radiation exposure was thus avoided.

Residual Primary Tumor. Occasionally,

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* Armour Thytropar.

tumor will be known to be residual in the primary site, even after a skillful dissection. Since the majority of deaths due to differentiated thyroid carcinoma results from local extension and invasion, such remnants must be extirpated, but in such a manner as to produce the least disability. Two cases are cited in which it appeared wise to employ radioactive iodine for this purpose:

Patient v was a 9 year old boy who had developed a visible left lateral neck lymph node at about the age of 7 years. Although it varied in size with upper respiratory infections, the lymph node slowly became larger and in October, 1960, the patient's parents brought him to a surgeon for consultation. On October 17, 1960, during an exploratory operation, frozen section examination of tissue from the left lobe of the thyroid gland and from left cervical lymph nodes gave evidence of the presence of papillary and follicular adenocarcinoma. Full exploration of the neck then revealed a large tumor which involved the left lobe of the thyroid gland, and which had apparently metastasized to a number of lymph nodes in the jugular chain. Lymph nodes in the right side of the neck were sampled but did not contain tumor. The neoplasm was found to have extended through its capsule posteriorly and directly into the wall of the esophagus. Esophageal extension was removed, and the tumor was dissected off the surface of the subglottic trachea. Tumor extended along both recurrent laryngeal nerves, which were dissected free. All normal thyroid gland which could be identified was removed, but the operation was terminated at this point with the knowledge that residual tumor tissue was present in the right thyroid area, and possibly in certain adjacent lymph nodes. Postoperatively, there was transient hypoparathyroidism, and also bilateral vocal cord paresis which was treated with a skin tracheostomy.

The patient was then referred to the Radioisotope Laboratory. We found him to be a healthy, vigorous-appearing young boy with a healing thyroidectomy scar. The tracheostomy was still patent, and was required because of the persistent vocal cord paresis. There was a diffuse, slightly indurated, ill-defined soft tissue mass in the right thyroid region, and there were a few palpable lymph nodes along the right sternocleidomastoid muscle. A tracer dose of 50 μc of I^{131} as sodium iodide was given orally, and 5 units of TSH were administered intramuscularly. Directional counting with a hand probe and scintillation scanning showed evidence of the presence of considerable activity overlying the thyroid cartilage and extending into the soft tissues of the neck on the right side (Fig. 1, *A* and *B*). A lesser amount of activity was found about the skin tracheostomy site. The referring surgeon stated that to the best of his belief the remaining tissue could not possibly be normal thyroid gland but must represent residual tumor. He further stated that he did not wish to re-explore the neck and asked that radiotherapy of some sort be undertaken. An additional tracer dose of 50 μc of I^{131} was given and a 48 hour urinary excretion test was begun. Only the first 24 hour sample was delivered for counting, but it contained 68 per cent of the administered dose, when allowance had been made for residual radioiodine content. Retention of 32 per cent of the tracer dose in 24 hours, much of which seemed to be localized in the neck, promised a good therapeutic result with radioiodine (Table v). The extent and distribution of tumor presumed still to be present in the neck were such that heavy irradiation of the lower cervical spine and cord might have been unavoidable with external beam techniques. After weighing all the considerations described above, a treatment dose of 22.9 mc of I^{131} was given by mouth on November 22, 1960, following the administration of 10 units of TSH. By December 30, most of the activity had disappeared from the primary site and lymph nodes.

In late February, 1961, about 3 months after radioiodine treatment, the diffuse mass was no longer palpable in the right thyroid region, the pattern of lymphadenopathy in the neck was a usual one for a young boy, and full vocal cord function had returned bilaterally. The skin tracheostomy was closed shortly thereafter and, because of incipient deep hypothyroidism, replacement was instituted using thyroid extract and, later, l-thyroxine. The patient has been seen at the usual 3 month intervals, and physical examination, roentgenograms and tracer studies of the neck have remained within normal limits.

Comment. Using the information in Table vi which makes allowance for patient size, this young boy received a whole-body dose of about 20 rads from his single radioisotope treatment. The result thus far in a case of aggressive primary tumor is judged to have been worth this exposure.

A case featuring repeated postoperative recurrence of tumor follows:

When Patient VI was 5 years old, her parents became concerned about a growing lump which appeared on the left side of her neck. They were directed by the family pediatrician to a surgeon experienced in thyroid disease, and on January 9, 1957, an exploratory thyroidectomy was performed. A well-differentiated papillary and follicular adenocarcinoma of the thyroid gland was discovered and was found to be invading the soft tissues of the neck locally. Residual tumor was thought to be present in the left thyroid area and a course of conventional voltage, tangential beam roentgen-ray therapy was administered to this region postoperatively. The tumor exposure dose was of the order of 3,000 to 3,500 r.

Two years later, in March, 1960, lymph nodes became palpable on the right side of the neck, and the thyroid region was re-explored surgically. No residual primary tumor was found, but several lymph nodes in the right jugular chain were removed and were found to contain tumor.

Less than 1 year later, in January, 1961, nodules became palpable in the operative site on the right side of the neck, and a third operation revealed the presence of tumor recurrence. In intervals between operations and for 8 months after the last procedure, the patient was maintained on various levels of oral thyroid extract in an unsuccessful effort to suppress tumor growth.

In September, 1961, the surgeon felt that a third recurrence was present on the right side of the neck, and the patient was referred to the Radioisotope Laboratory for further study. When we first saw her, she was a pallid 8 year old girl, rather small for her age, but quite bright and mature. Soft, movable lymph nodes of small size were palpable on both sides of the neck. Roentgenographic studies showed no evidence of distant metastasis. A tracer dose of 50 μc of I^{131} was given together with an intramuscular dose of 5 units of TSH. Forty-eight hour urine collections were obtained and showed a retention of 26 per cent, much of which was identifiable in small areas along the surgical scar and over the lymph nodes bilaterally (Fig. 2). A therapeutic dose of 25.3 mc was given on November 13, 1961, together with additional TSH, and by February, 1962, all activity had disappeared from the lymph nodes and thyroid area. On follow up examinations since

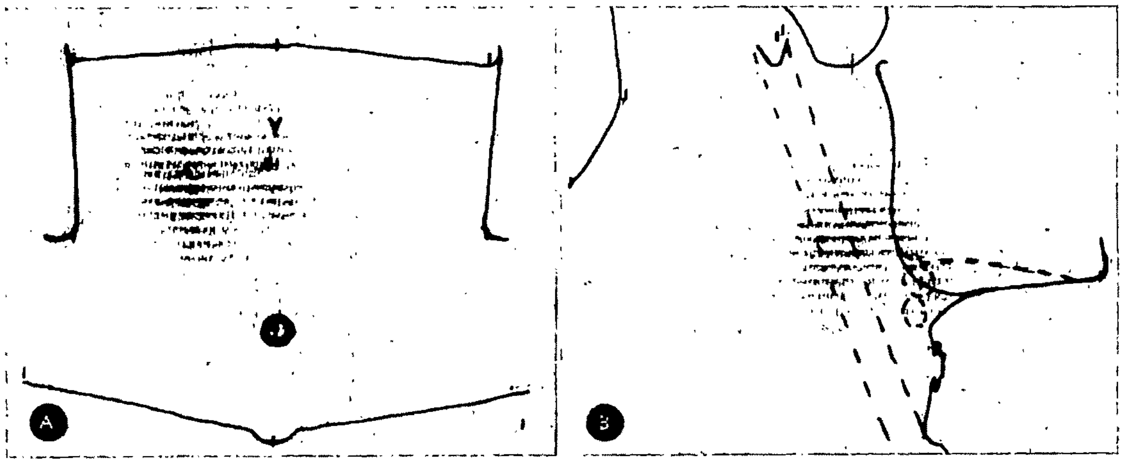

FIG. 1. Patient V. (*A*) Frontal scintillation scan of the neck. Solid lines from above downward represent line of the jaw, lateral margins of the neck, and superior margins of the clavicles. Concentric circles represent tracheostomy. Note concentration of I^{131} in residual primary carcinoma and lymph node metastases lateral and superior to the right thyroid area. (*B*) Right lateral scan of the neck performed at the same time as *A*. Solid lines represent pinna, mastoid process, posterior line of neck soft tissues, line of mandible, and anterior outline of neck including tracheostomy site. Dotted lines represent right sternocleidomastoid muscle, submandibular soft tissues and palpable nodules. I^{131} tracer is localized in residual primary tumor and metastatic lymph nodes.

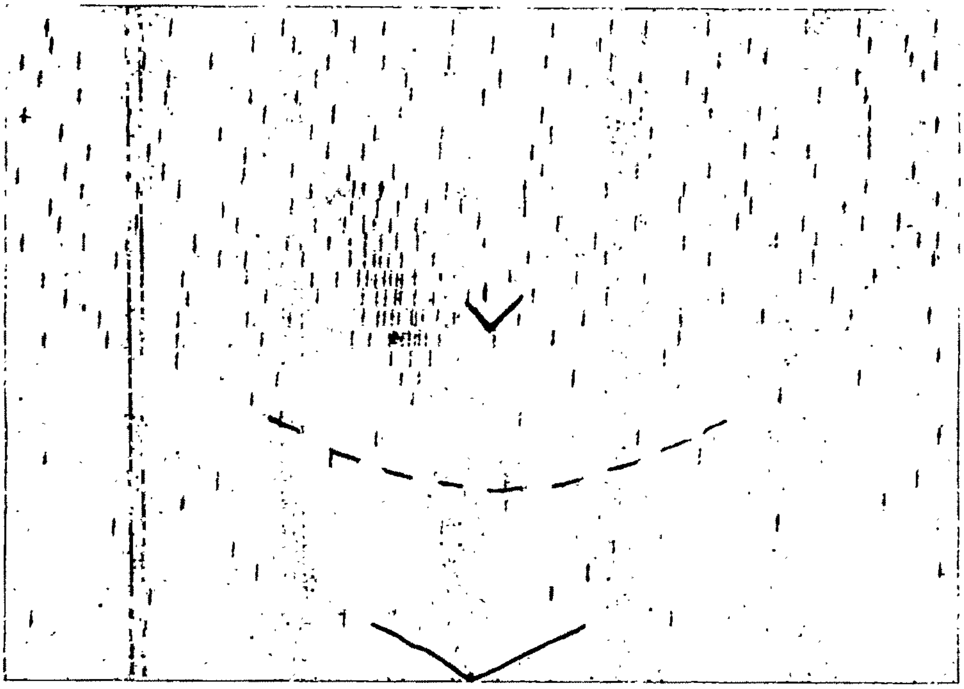

Fig. 2. Patient vi. Frontal scan of the neck. Solid lines from above downward represent angle of the thyroid cartilage and the suprasternal notch. Dotted line represents thyroidectomy scar. Note accumulation of tracer to the right of the thyroid cartilage in known recurrent differentiated thyroid carcinoma.

that time, there has been no evidence of specific accumulation of radioactive tracer, despite the transient development of cervical lymphadenopathy during colds.

Comment. In this case whole-body exposure was estimated by various means to be about 35 rads. Against this must be weighed the fact that the patient has now apparently been tumor-free for about 3 years, the longest such interval she has known since the initial operation. It is felt that treatment of residual tumor in the neck may have been of decisive value to this little girl.

The following is the case of an unusual primary tumor:

Patient vii was found to have thyroid cancer because of keen observation on the part of her school doctor, who noticed that she had small bilateral neck masses. To his surprise the girl's family told him that these had been present since birth. Palpation revealed them to be irregular and firm, and he thought that the upper portion of the mass along the right sternocleidomastoid muscle was adherent to the thyroid cartilage. He then referred the patient to a local hospital, where she was prepared for surgery with the tentative diagnosis of carcinoma of the thyroid gland with regional metastases. The operating surgeon identified a nodule lateral to the thyroid cartilage on the right side and a second one low in the neck just to the right of the suprasternal notch. These were removed and found by frozen section examination to be lymph nodes containing follicular carcinoma of the thyroid gland. The thyroid gland could not be identified, for all that could be seen in the midline was a thin, translucent membrane which had much the appearance of fascia and which covered the lower portion of the thyroid cartilage. So unusual was the aspect of this membrane that the surgeon terminated his operative procedure at this point in order to refer the patient to the Parkland Memorial Hospital Radioisotope Laboratory for additional study.

When first seen in our laboratory on December 10, 1960, the patient was a small, thin 10 year old girl who seemed quite keen and energetic despite the fact that she had recently had a major surgical operation. Chest and skeletal roentgenograms were available and showed no evi-

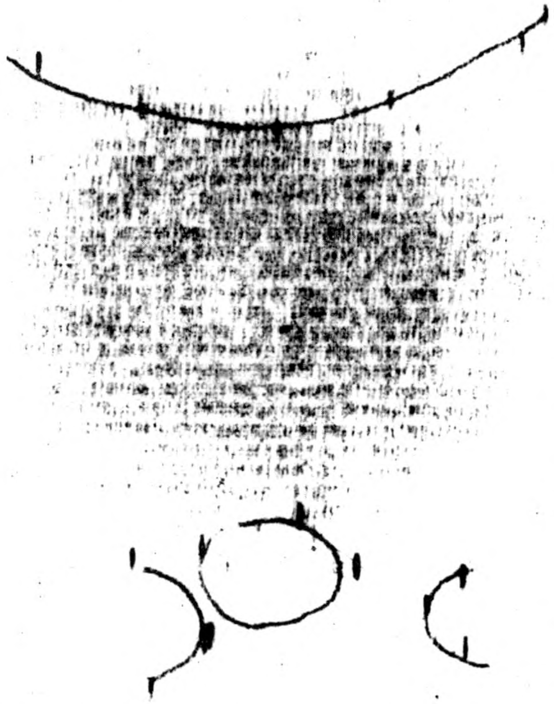

FIG. 3. Patient VII. Frontal scan of the neck. Solid lines from above downward represent line of recent surgical incision and the suprasternal notch and medial clavicular borders. Note the accumulation of I^{131} tracer in an unusual round pattern in the lower anterior cervical midline. At re-exploration, this represented a thin carpet of tumor over the lower thyroid cartilage and upper trachea, extending laterally and inferiorly.

dence of metastatic disease. A tracer dose of 100 μc of radioactive iodine was given by mouth. On the following day all of the detectable isotope seemed to be in an unusual configuration in the midline, and a scan was made (Fig. 3). Tracer was concentrated in a remarkable round pattern which bore no resemblance to the ordinary configuration of the thyroid gland. No tracer was detectable over any of the palpable lymph nodes in the neck. It seemed likely that the radioiodine had been deposited in functioning tumor, and so a second operation was performed.

The second exploratory thyroidectomy was performed on December 14, 1960, and the fascia-like membrane was found to cover a thin carpet of tumor tissue which completely covered, and was intimately adherent to, the anterior surface of the thyroid cartilage inferiorly. The tumor extended inferiorly along the trachea and entered the thoracic inlet. A number of lymph nodes was removed from both sides of the neck, and some of them had to be dissected free from the strap muscles. The surgeon felt that he had had to leave residual tumor both in the primary area and about some of the lymph node sites.

The patient was next seen in the Radioisotope Laboratory on February 13, 1961, at which time she had convalesced satisfactorily from her second operation and appeared to be in good condition. A few lymph nodes were palpable in the left side of the neck, and the surgical scar was healing nicely. An oral tracer dose of 100 μc of radioiodine was administered and directional counting showed evidence of activity over the thyroid cartilage, within a palpable lymph node in the anterior triangle on the left side, and over a previously undetected lymph node in the left posterior cervical region. Forty-eight hour urine excretion was 85 per cent, but much of the iodine retained in the body seemed to be concentrated in the palpable lymph nodes. Accordingly, an effort was made to enhance tumor localization of isotope and the patient received three consecutive daily intramuscular injections of 10 units of TSH. The urine was collected for 24 hours to determine residual urine radioiodine level and a second tracer dose was administered. Urinary excretion of iodine was now reduced to 77 per cent for a 48-hour period, and of the 23 per cent retained in the body almost all could be accounted for in the small lymph node deposits. Again, external beam therapy did not seem feasible and isotope treatment was elected. Because of the low concentrations in many individual areas, we decided to employ a somewhat larger treatment dose than is customary and so 50 mc of I^{131} was administered on February 24, 1961.

By April 3, 1961, radioactivity had disappeared and lymph nodes were less readily palpable. By then the patient exhibited signs of hypothyroidism and replacement was instituted with thyroid extract. In 3½ years since that time, the patient has not developed evidence of persistence in the primary site or of a new metastasis, either in the neck or any other part of the body.

From tumor and blood disappearance data

the whole-body radiation dose is estimated to have been 45 rads.

Comment. Because of the ominous characteristics of the primary tumor, in this case some form of post-surgical treatment was mandatory, and it is gratifying that there has been no local recurrence of tumor. As it has in a number of other cases, thyroid stimulating hormone proved useful in enhancing tumor concentration of radioisotope.

The following case is one in which the need to use radioiodine is debatable:

Patient VIII was a 15 year old girl who, in July, 1956, entered the Parkland Memorial Hospital Outpatient Clinic complaining of a 6 month history of enlarging goiter. On physical examination a nodule was indeed found in the right thyroid lobe and a thyroidectomy was performed. All thyroid tissue was removed except for that about the spared parathyroid in the right lower pole. A diagnosis of mixed papillary and follicular carcinoma was made from the surgical specimen. Early follow-up was incomplete but radioisotope studies and roentgenograms gave no evidence of recurrence or distant spread. On February 19, 1958, however, the patient was seen in the Radioisotope Laboratory, and a scan was obtained which revealed the presence of tracer concentration not only in the thyroid remnant but in a large focus near the angle of the mandible on the left side (Fig. 4, *A* and *B*). Repeated palpation failed to evoke a definite mass. There was only a sensation of deep fullness in the neck. The surgeon in charge of the case declined to re-explore the neck and suggested a trial of tumor suppression with thyroid extract, a technique widely practiced at that time. Interestingly enough, replacement medication had never been started and had never been required. This ominous fact alone might have led to earlier discovery of functioning neoplasm. For a brief time the patient was given 6 grains of thyroid extract a day, but although dosage was reduced to 4 grains per day she was quite uncomfortable throughout the 3 month suppressive trial. To our surprise radioiodine accumulated readily in the residual thyroid and metastatic lymph node in a tracer test performed 2 weeks after discontinuance of thyroid extract. Suppressive therapy was then per-

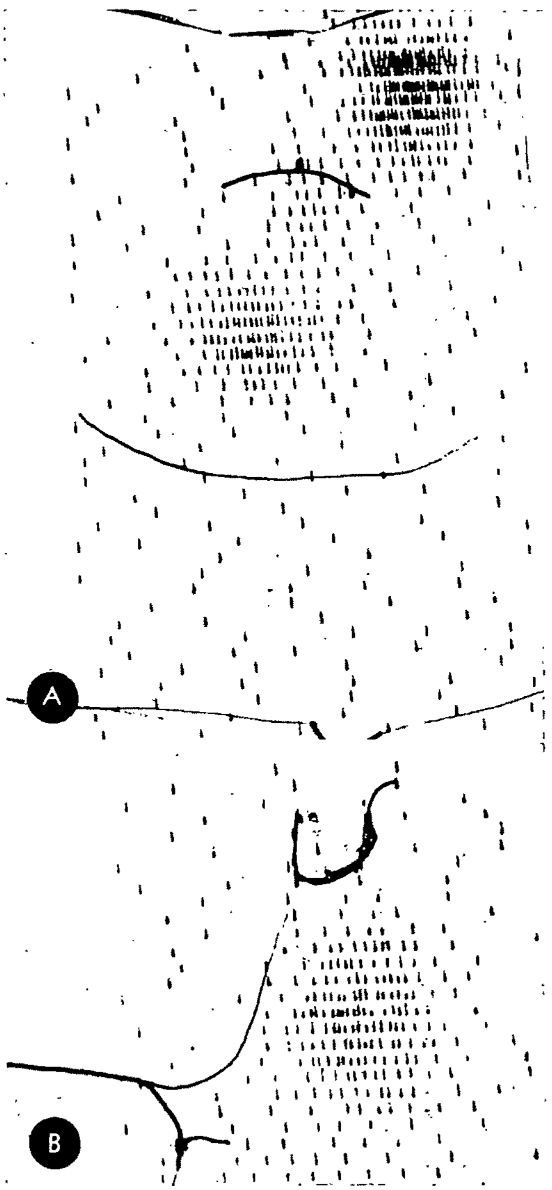

Fig. 4. Patient VIII. (*A*) Frontal scan of the neck. Solid lines represent from above downward outline of the jaw, superior margin of the thyroid cartilage, surgical incision, and line of the clavicles and suprasternal notch. Note concentration of I^{131} tracer in remnant thyroid about a spared parathyroid in the right lower pole region. Note also concentration of tracer in presumed lymph node metastasis near the angle of the mandible on the left side. (*B*) Simultaneous lateral scan. Solid lines denote ear lobe, line of the jaw and outline of the upper neck anteriorly. I^{131} is localized sharply in presumed lymph node metastasis.

manently discontinued in the hope of enhancing uptake of radioiodine in the area of interest, although a normal, TSH-dependent mechanism did not seem to be present. Six weeks after withdrawal of thyroid extract, 24 hour iodine retention was 18 per cent measured by the excretion method, (82 per cent excretion) and at 3 months retention was 37 per cent in 24 hours. At this point, a 100 mc dose of I^{131} was given orally.

Within 2 months activity had disappeared from both foci, and 4 months after treatment the patient began to exhibit signs of hypothyroidism. Replacement medication was instituted with thyroid extract, and later l-thyroxine was substituted. Neither of the areas in the neck has ever accumulated radioiodine again. The patient remains well at this time, with no evidence of disease.

A whole-body dose of 50 rads has been estimated.

Comment. In this case one might argue with some justification that the patient could have been spared whole-body radiation exposure by what might have been a relatively simple operative procedure. Although this option was not available to our patient at the time, the radiotherapist might well be within his rights to press the surgeon to undertake re-exploration in circumstances of this sort, especially when they involve a child.

Alternatives might have been either to withhold treatment until local growth of metastases produced a life-threatening situation, or to attempt extirpation of the metastasis with external beam radiotherapy. In a child of this age, growth disturbances are not apt to be a problem, and it would not have been necessary to include the cervical spinal cord in the treatment volume. On the other hand, the patient had attained relatively full adult growth, and so the whole-body radiation dose from I^{131} was considerably less than it would have been in a smaller child.

TREATMENT OF DISTANT METASTASES

Patient x slowly developed cyanosis and difficulty in breathing, in 1940, when he was 14 years of age. He was referred to a large hospital where some sort of mass in the neck was removed for biopsy examination, and a diagnosis of cancer may have been made. Medication with a course of Lugol's solution was undertaken and the patient's state is said to have improved. When he returned to the same hospital 3 years later, however, lymph nodes were palpable on both sides of the neck, and on this occasion the removal of one of them yielded the unequivocal diagnosis of papillary carcinoma of the thyroid gland. Roentgenographic examination of the chest gave evidence of the presence of disseminated nodular metastases. A course of external beam radiotherapy of unknown modality was delivered to the neck to an exposure dose of approximately 3,000 r.

The patient remained well for about 7 years, but at the age of 24 years he noted the abrupt onset of dyspnea and cyanosis, and, for the first time, he had episodes of hemoptysis. He then reported to the University of Arkansas Hospital, where the diagnosis of carcinoma of the thyroid was confirmed by cervical lymph node biopsy, and the first of many radioiodine treatments was given. Over the period of the next 7 years, a total of 402 mc of I^{131} was administered in 5 treatment doses. In the course of a comprehensive study of this patient, Pierce and his associates[17] investigated the persistent cyanosis and determined that pulmonary arteriovenous fistulas were present, presumably within one or more of the metastatic lesions. Vital capacity and arterial hemoglobin oxygen saturation studies were performed (Table IV) before and 7 months after the administration of one of the later therapeutic doses of iodine and showed significant improvement in these variables.

The patient then moved to the vicinity of Dallas and was referred to the Radioisotope Laboratory at Parkland Memorial Hospital. When first seen here, the patient was a 34 year old man who seemed thin and somewhat undernourished, and who exhibited cyanosis of lips and nail beds as well as finger clubbing. Chest roentgenograms (Fig. 5*A*) showed a disseminated, finely nodular infiltration characteristic of hematogenous pulmonary metastases from carcinoma of the thyroid gland. Fullness of the hilar shadows and mediastinum has never been entirely solved, but might represent, in part, metastases to mediastinal lymph nodes. A comparison of our initial roentgenogram with those made in the past showed no change to have occurred in the extent or distribution of the oft-treated tumor over a period of about 10 years.

TABLE IV

STUDIES PERFORMED ON PATIENT X BY PIERCE *et al.*[17]
AT THE UNIVERSITY OF ARKANSAS HOSPITAL

Date	Vital Capacity		Total Lung Capacity	Ratio of Residual Volume Lung Capacity	Mixing Index*	Arterial Hemoglobin Oxygen Saturation	
	Total	1-Seg.				With Patient Breathing Air	After Breathing of Oxygen for 20 Min.
1957	liters	%	%	%	%	%	%
Jan.	3.65	—	5.61	35	0.88	73	85
Aug.	4.45	86.0	6.81	35	0.93	85	99

* Note improvement in vital capacity and arterial oxygen saturation attributed to treatment with radioactive iodine.

There was no important finding in the neck. The patient's only complaint was a slow but progressive return of dyspnea on exertion during the past 3 years. A tracer dose of radioactive iodine was localized so sharply in the pulmonary metastases that a photoscan of the lung fields (Fig. 5*B*) was easily obtained. Forty-eight hour retention of an administered dose of radioiodine was 35 per cent, a satisfactory value (Table v). On questioning we found that the patient had not been taking thyroid replacement medication for some time, and had apparently been maintained in the euthyroid state by hormone produced by his tumor. The only treatment available seemed to be I^{131}, but the danger of producing pulmonary fibrosis was now added to that of possible induction of leukemia, and these had to be weighed against the possibility of giving symptomatic relief from severe respiratory difficulty. After consultation with the patient about possible consequences, he elected treatment and 100 mc of radioiodine was given, but only partial symptomatic relief was gained. Six months later an additional 54 mc dose was administered. The patient's respiratory symptoms then slowly subsided and have remained in abeyance for 4 years. Further, the patient finally became hypothyroid, and re-

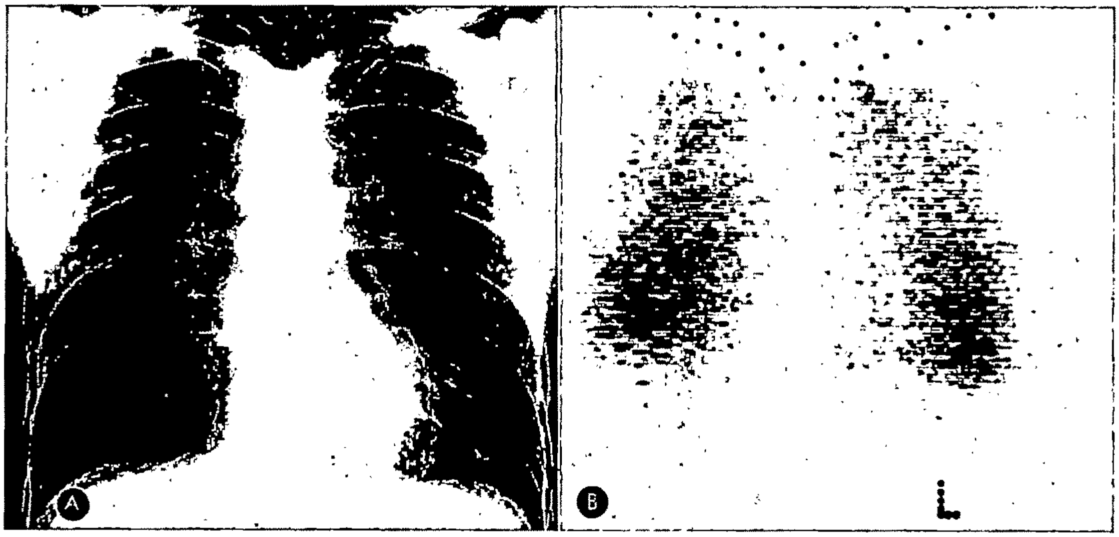

FIG. 5. Patient x. (*A*) Upright posteroanterior roentgenogram of the chest made in 1960. Comparison with studies made elsewhere over the previous 10 years showed no change to have occurred in the appearance or extent of the disseminated, nodular metastatic process involving both lungs, nor of the prominent lymph nodes in the hilar and right paratracheal regions. (*B*) Scintillation scan of metastatic deposits in the lungs made after the administration of a tracer dose of I^{131}.

TABLE V

24 AND 48 HOUR I^{131} URINARY EXCRETION TEST*

	Excretion		Retention	
	24 hr.	48 hr.	24 hr.	48 hr.
Athyreotic Value	85–95%	90–95%	5–15%	5–10%
Therapeutically Favorable Value	<70%	<80%	>30%	>20%

* Values are given both for athyreotic individuals and for patients with differentiated thyroid carcinoma in whom a favorable response to radioiodine treatment might be expected on the basis of past experience. Excretion is measured against a 100 per cent standard and the 48 hour value is the sum of the content of two consecutive 24 hour collections. Retention figure is obtained by subtracting 24 or 48 hour value from 100 per cent.

placement medication with l-thyroxine was started. Further treatment with radioactive material has not been necessary, but if respiratory symptoms return and do not appear to be the product of radiation fibrosis of the lung, we will have no choice but to offer isotope treatment once again. Radiation exposure, which may be assumed to have been delivered over a 10 year period from 1950 through 1960, may be as much as 250 rads to the whole body. There is no way to estimate lung dose.

The following case presents several unusual circumstances, one almost unique in the annals of nuclear medicine:

Patient XI, at the age of 14 years, was first noted by relatives to have a goiter, which, upon examination in the Outpatient Clinic was found to represent a large solitary nodule in the left lobe of the thyroid gland. The patient did not return to the Clinic until 8 months later, but she then consented to undergo thyroidectomy. On March 15, 1956, most of the thyroid gland was removed, although a certain amount of thyroid tissue was spared about a parathyroid gland in the left upper pole region. Lymph node metastases were not apparent at that time and lymphadenectomy was not performed. It was thought that residual tumor was still present in the primary site and radiation therapy was given to the thyroid region with 250 kv. peak, 3 mm. Cu half value layer, employing a multiple port technique, to a dose of about 3,500 r.

The patient was then lost to follow-up and was first seen by us on June 18, 1958, more than 2 years after operation and radiotherapy. Although she had not been taking any thyroid replacement medication, she was not hypothyroid, and so tracer tests were undertaken to discover the nature and magnitude of the functioning thyroid tissue which obviously must be present. Not only was residual tissue identified at the left upper pole, but an unusual localization was obtained in an area (Fig. 6,*A* and *B*) which corresponded to the base of the tongue. Indirect mirror inspection of the tongue and hypopharynx and palpation of the base of the tongue did not show a lingual thyroid, nor did they disclose any mass. Repeat tracer examination again gave the scan evidence seen in Fig. 6,*A* and *B*. In addition, there was more radioactivity detectable over the lungs than could be accounted for by the lung blood pool alone. Chest roentgenograms gave no evidence of metastatic disease, however. A 48 hour urine study showed a satisfactory radioiodine retention of 30 per cent (Table V). Most of this activity could be quantitated in the remnant thyroid gland and in whatever lesion was present in the base of the tongue, whether persistent lingual thyroid or carcinoma in a lymph node. A treatment dose of 100 mc of I^{131} was administered, and the patient was again lost to follow-up, this time for a period of about 18 months.

When the patient returned on December 16, 1959, she appeared to be pale, weak and ill, but she was not hypothyroid. On this occasion radioactive iodine did not localize on either side of the neck, and both had apparently been ablated. Instead there was distinct localization of tracer over the lung fields of such a magnitude that a scan (Fig. 7*A*) could be obtained. A posteroanterior roentgenogram of the chest (Fig. 7*B*) made at that time again showed no evidence of the presence of metastatic disease. Urinary excretion study could only be carried out for 24 hours, but showed a 30 per cent retention, much of it accountable in the lungs.

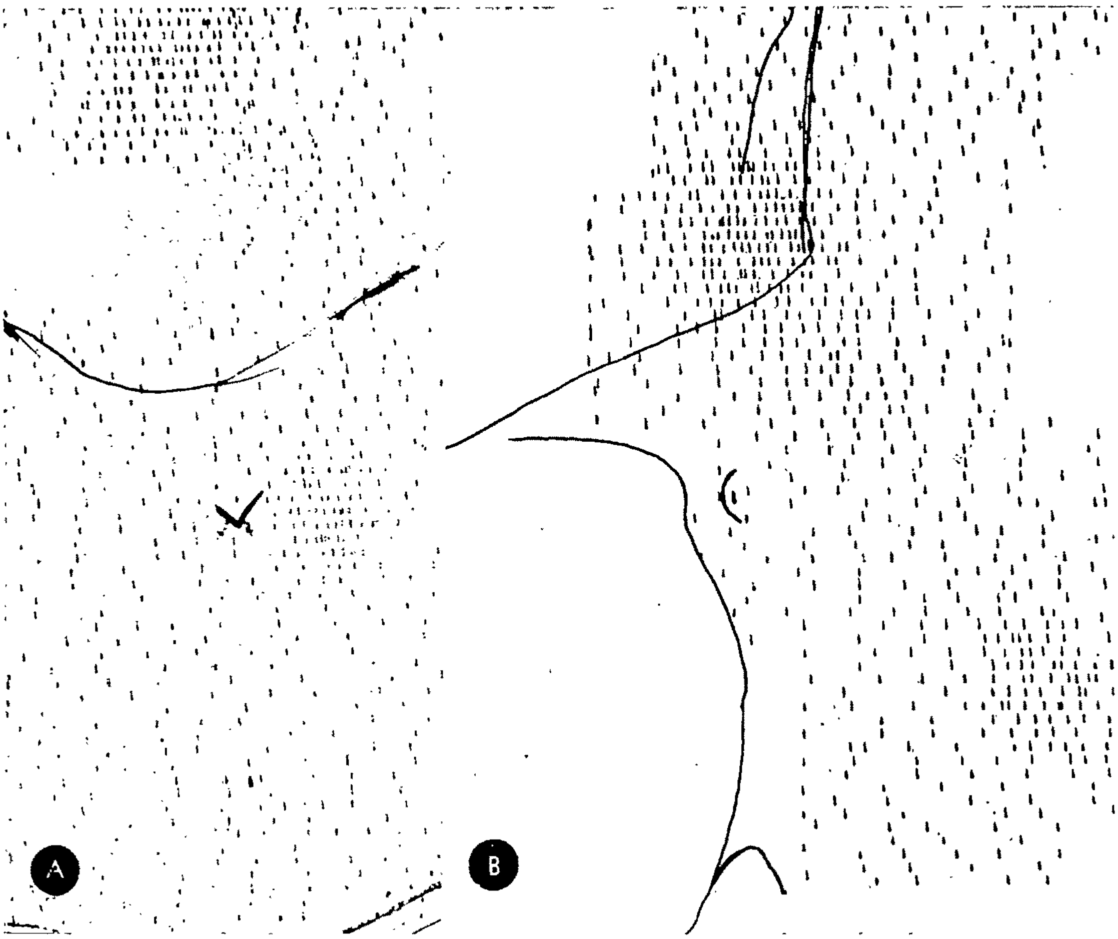

Fig. 6. Patient xi. (*A*) Frontal scan of the neck, 1958. Solid lines represent from above downward outline of the mandible and outline of the clavicles. Note localization of I^{131} tracer in the region or spared parathyroid tissue in the left upper thyroid area and an unusual deposit in high cervical midline or base of tongue. (*B*) Simultaneous lateral scan of the neck. Solid lines represent outline of the mandible and anterior surface of the neck. Note again upper deposit of I^{131} tracer in an area corresponding to that of the base of the tongue. No lesion could be demonstrated there by indirect laryngoscopy or manual palpation.

Disseminated micronodular pulmonary metastasis is one of the common patterns of carcinoma of the thyroid and sometimes the nodules are so small as to be barely perceptible. In several cases reported in the literature,[3,6] they have been so small as to escape roentgenographic detection even in the aggregate. We felt this was such a case, and that we were obliged to accept the scan as sole evidence of the presence of metastasis. Further questioning of the patient revealed that she had had subtly progressive difficulty in breathing and had suffered dyspnea upon exertion. Even though we had given a rather large dose of radioiodine to a young person only 1 year before, we felt that we had little to offer this patient other than additional isotope treatment. Accordingly, she was again hospitalized and an 85 mc dose of I^{131} was given on December 30, 1959, and within 4 months selective pulmonary localization of iodine disappeared (Fig. 7*C*).

Once again the patient disappeared, and despite our efforts we could not locate her for follow-up. She returned almost 2 years later, now giving satisfactory symptoms and signs of the hypothyroid state. Once again chest roentgenograms failed to offer any evidence of metastatic disease, but they did show considerable enlargement of the cardiac silhouette (Fig. 8*A*—compare with Fig. 7*B*). An I^{131}-cholografin blood pool scan (Fig. 8*B*) demonstrated a voluminous pericardial effusion.[2]

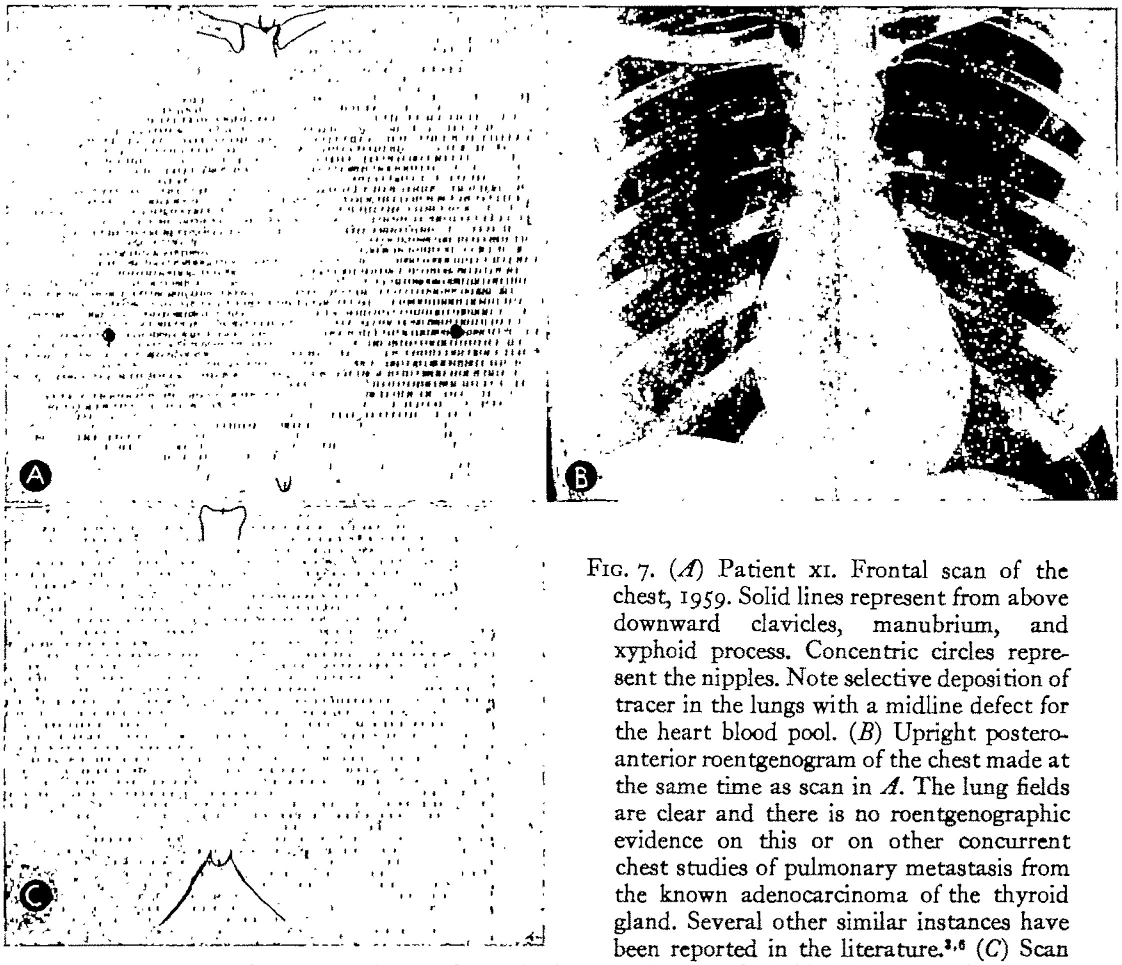

Fig. 7. (*A*) Patient xi. Frontal scan of the chest, 1959. Solid lines represent from above downward clavicles, manubrium, and xyphoid process. Concentric circles represent the nipples. Note selective deposition of tracer in the lungs with a midline defect for the heart blood pool. (*B*) Upright posteroanterior roentgenogram of the chest made at the same time as scan in *A*. The lung fields are clear and there is no roentgenographic evidence on this or on other concurrent chest studies of pulmonary metastasis from the known adenocarcinoma of the thyroid gland. Several other similar instances have been reported in the literature.[3,6] (*C*) Scan of lung fields in March, 1960, no longer shows significant evidence of specific deposition of tracer in presumed pulmonary metastatic lesions following treatment with I^{131}.

We found that the patient had spent the intervening 2 years in a mental institution and while there she had not received any thyroid medication. Replacement was instituted with l-thyroxine, and the pericardial effusion slowly receded, while the cardiac silhouette returned to normal in size. The patient has been followed regularly for the past year and at the present time there is no evidence of residual disease. She remains in the euthyroid state by virtue of the administration of 200 μg. of l-thyroxine per day.

The whole-body radiation dose has been estimated at about 80 rads over a 2½ year period.

Comment. Although none of the members of this small group can be said to have been cured of the disease at this early date, immediate local recurrence seems to have been prevented, and persistent disease, regardless of its location, seems to have been brought under control.

DISCUSSION

There is a need for a coherent approach to each kind of entity with which the radiotherapist must deal. The following suggested scheme is drawn from experience in this laboratory and in others. It certainly cannot be applied rigidly to the individual case, but is intended to be a general method of management of differentiated thyroid cancers in children.

It is always desirable for the radiotherapist to examine in advance any patient for whom postoperative treatment may be

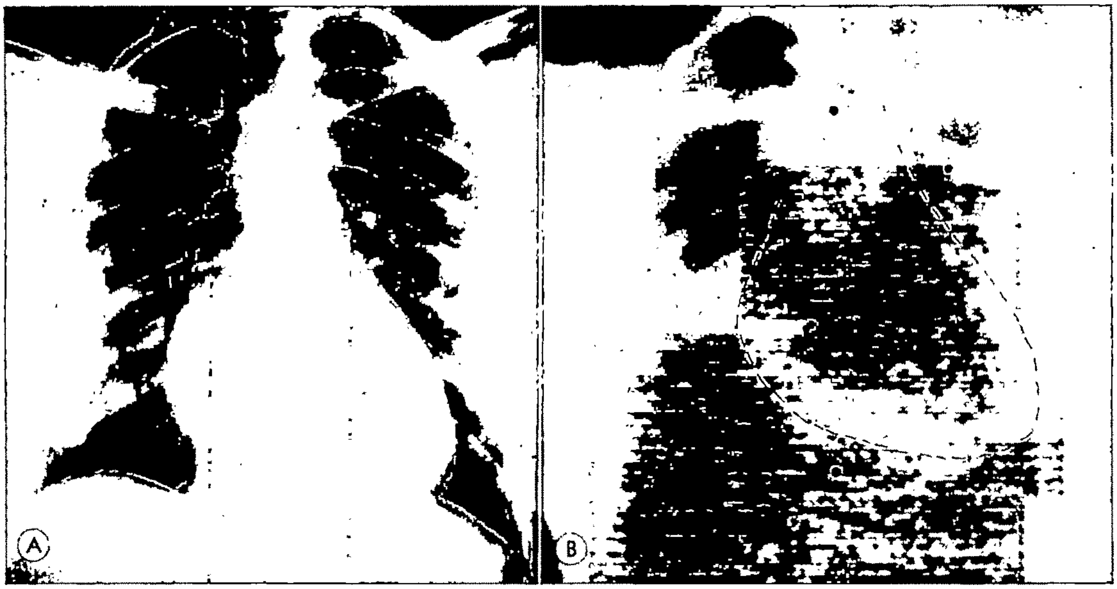

FIG. 8. Patient XI. Upright, 6 foot, posteroanterior roentgenogram of the chest made in 1961, when patient returned for follow-up in a deeply hypothyroid state. Note large cardiac silhouette and compare with normal silhouette seen on a roentgenogram (Fig. 7*B*) made 2 years earlier. (*B*) Photoscan record of data from I^{131}-cholografin blood pool scan imprinted on simultaneously exposed 7 foot, mid-respiration, anteroposterior recumbent chest roentgenogram. Clear belt about heart blood pool, best seen between the blood pool and accumulation of tracer in liver, indicates the presence of a voluminous pericardial effusion, as does discrepancy between size of heart blood pool and size of cardiac silhouette (dotted line). (By permission of the *Southern Medical Journal.*)

needed. In the case of thyroid cancer, this may be accomplished more often than usual, for the radiologist may participate in the general work-up which leads to the identification of the neoplasm. If the disease presents as a solitary nodule, a radioiodine scan is usually obtained. Only a nodule which functions so energetically as to suppress the activity of the remainder of the thyroid gland is considered a "hot" nodule in this department. This represents the only type which is safe to observe over a period of time, but nodules of high specific activity seldom occur in childhood, and so the problem of prolonged observation of a nodule in the thyroid gland of a child rarely need be faced. There is a material chance of cancer being present in any other kind of nodule, especially in children.

Preoperative tracer tests may serve to identify metastatic thyroid adenocarcinoma in palpable lymph nodes and they may also reveal the presence of differentiated tumor in locations which are not obvious upon clinical examination. Some of these, if demonstrated by tracer techniques, may prove to be surgically accessible at the time of thyroidectomy, however.

Under favorable circumstances the radiotherapist may also be able to visit the operating room during thyroidectomy to view the primary tumor, and, together with the surgeon and pathologist, he should examine the slides made from the primary tumor and its extensions. It is possible to predict the behavior of a tumor from the appearance of microscopic sections, for if follicles are present, and if they contain colloid, however faintly it may be stained, there is an excellent chance that the tumor and its metastases will either spontaneously take up a good deal of radioactive iodine, or may be made to do so.

If an undifferentiated cancer is found, postoperative treatment should be started as soon as possible, but, if a differentiated tumor has been removed and if follicular elements are present within it, as is usually the case, then there is no need for haste unless residual tumor is known to be present in a life-threatening location. An interval of 6 weeks to 3 months between time of operation and the first attempt to measure incorporation of isotope in the tumor is desirable. During this time the patient should not receive replacement thyroid medication, although there is still an unfounded belief in some quarters that it is dangerous to permit a patient with differentiated thyroid carcinoma to go for even the shortest period of time without thyroid hormone, for fear of wild and rapid tumor growth. This never happens with differentiated tumor, and, even if it did, the process could not be controlled with thyroid hormone. The hormone will, however, block trapping and binding of iodine by thyroid remnants and metastases, and so must be avoided until the possibility of the need for isotope radiotherapy has been dismissed.

At 6 to 12 weeks following surgery a tracer dose in the range of 50 to 200 μc of I^{131} as sodium iodide is given by mouth, both to act as a tracer for localization of tumor tissue and also as the tracer dose for a 48 hour urine retention study. In this laboratory we employ for tumor search a small hand-held scintillation probe with a collimated ½ inch thallium-activated sodium iodide crystal. The output of this probe is registered by a counting rate meter which has an audible tone scale. The head and neck area is mapped with the probe and the location of spared thyroid remnants is determined, together with the presence or absence of tracer in areas of known residual primary tumor, or in suspected lymph nodes. Counts are also made over lungs and liver and over any suspicious areas present in the roentgenographic skeletal survey. If there is a sufficient amount of radioactivity in any area, a scan record is made with a modified commercial scanning apparatus.

At the time the tracer dose is made up, a 100 per cent standard is also prepared for use in the 48 hour excretion study. Two consecutive 24 hour urine samples are collected, beginning with the time of the administration of the tracer dose. The Radioisotope Laboratory issues the collection bottles, which are of one liter capacity, and of identical size and shape. When the two 24 hour collections have been returned for counting, they are made up to equal volume by adding water to the less voluminous of the pair of samples. The 100 per cent standard is then placed in a third collection bottle and is diluted to the same volume as each of the two 24 hour specimens. While aliquot samples may be taken from the standard and the two test volumes, it is easier, and about as accurate, to count by placing each bottle in a standardized location with respect to the mouth of a large crystal well-counter. The volumes counted are the same and the geometries involved are the same. Total excretion is thus the product of addition of the per cent recoveries in each of the two 24 hour samples. The standards for this test are summarized in Table v.

The essentially athyreotic individual, adult or child, will excrete about 85 to 90 per cent of a tracer dose of radioiodine in 24 hours, and about 90 to 95 per cent in 48 hours. Thus body retention of iodine will amount to from 5 to 10 per cent in an athyreotic patient over a 48 hour span. Experience has shown us that it is worthwhile to consider the therapeutic use of iodine if whole-body retention is at least 30 to 40 per cent in 24 hours or from 20 to 30 per cent in 48 hours, and if directional counting shows retained isotope to lie principally in remnant thyroid and suspected metastases.

Depending upon the results of these tests one of two courses of action may be taken: (1) If there is no evidence of significant tumor at this time, replacement medication with thyroid extract or l-thyroxine may now be instituted. (2) If, however, there is known to be residual tumor but there is little or no accumulation of radioiodine in it and if body retention values are not in the promising range (Table v), an attempt to augment uptake by artificial means is justifiable, since the activity of even a small amount of remaining normal thyroid tissue may be sufficient to suppress thyroid-like behavior of metastases from a differentiated tumor. (We also use the following enhancement technique for study of those patients who are first referred to us after thyroidectomy and who are already receiving maintenance doses of thyroid hormone.)

In the past the administration and withdrawal of a blocking drug sometimes yielded good results in improving tracer uptake, but this is a time-consuming process and does not improve upon the results we have been able to obtain with thyroid stimulating hormone (See Case VII above). The daily dose, 5 units in a small child to 10 units in a larger child or adolescent, is given intramuscularly each day for 3 consecutive days. Although sensitivity reactions to TSH have been described, we have never encountered one. With the second dose a 24 hour urine collection is started, and with the third dose of TSH a radioiodine tracer is given. The preliminary urine specimen is used to determine residual iodine excretion, for which allowance must be made during the 48 hour excretion test. If the interval between tests is a lengthy one, the residual urine determination can be omitted, but if the interval is a matter of a few days, there may still be significant tracer content, even in an individual presumed to be athyreotic. If the results of this re-evaluation fail to show significant whole-body retention of tracer and definite localization in tumor, then the decision to use external beam radiotherapy or not will again depend upon the distribution of the tumor. If, however, there is now sufficient retention and localization of radioiodine to promise a good therapeutic result (Table V), a treatment dose can be given.

The radiotherapist has now brought himself to the point at which he must decide whether to advise the use of radioactive isotope treatment in a suitable case. There is no easy way to resolve the dilemma, but, in general, the growth disturbances which external beam therapy might produce in the cervical spine, larynx and trachea of a small child must be weighed, together with the possibility of radiation damage to the central nervous system. If these can be avoided in an individual case, then external beam treatment might be indicated regardless of age. If central nervous system injury seems likely, then radioisotope therapy would seem to be indicated regardless of the risk entailed in whole-body radiation exposure.

Before the treatment dose of radioiodine is given, the radiologist must discharge one last major responsibility. He must confer with the patient's parents and acquaint them with the nature of their child's disease, and also with some of the consequences of radiation exposure. This must be done carefully, in view of the fact that information pertaining to the development of leukemia and future generation genetic defects is not solidly grounded in proven fact. Having secured parental permission and having administered a therapeutic dose of radioiodine to a child, the radiologist is committed to a case which he must follow for a period of many years into the future. On the basis of the behavior of the tumor alone, follow-up in excess of 10 years would be required. Another cogent reason is that legal liability to a patient treated as a child usually extends at least to the patient's 21st birthday, or a year or 2 beyond in most states.

In selecting the size of the therapeutic dose of radioiodine to be used, a limiting factor may be imposed in the form of projected whole-body radiation exposure. This may be rapidly estimated in advance for patients of average sizes from the data in Table VI, which are based on our own experience, and also take cognizance of the recent work of Seltzer *et al.*[25] We, ourselves, attempt to keep whole-body dosage less than 25 rads in children under the age of 10 and less than 50 rads in children, adolescents and young people above the age of 10.

Strict radiation protection precautions are, of course, observed during and after the delivery of the therapeutic dose.

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Table VI

APPROXIMATE WHOLE-BODY DOSES OF RADIATION IN RADS PER MILLICURIE OF I^{131} ADMINISTERED ORALLY AS SODIUM IODIDE*

Age	5 Years	10 Years	15 Years	Man
Body Weight (kg.)	20	35	50	70
Rads per mc I^{131}	1.5	0.8	0.55	0.45

* Values are given for various weights by age. For intermediate ages and weights, one may interpolate between the given values.

Immediate follow-up includes patient visits to the Radioisotope Laboratory at 2, 4 and 6 weeks after the delivery of a therapeutic dose. A minor complication sometimes observed during this period, which causes no difficulty if understood in advance, is the development of slight soreness in the throat on swallowing which may occur if there is a significant amount of isotope-containing tissue in the thyroid region. At 4 to 6 weeks, and occasionally somewhat later, the early signs of hypothyroidism should begin to develop. The earliest of these is usually a subtle swelling of the soft tissues of the lower lids, noticed principally in the early morning. This may be followed rapidly by slight skin coarsening, with nail and hair changes appearing rather late in children.

If the patient becomes hypothyroid between 6 and 12 weeks after treatment, replacement medication can be given. The level is usually determined on a trial and error basis, for there is no way to predict the thyroid hormone requirement of a child. The failure of early signs of hypothyroidism to develop, however, is a warning of residual active thyroid tissue, and an energetic search should be undertaken to locate it, and to appraise it for further treatment. As is well known, metastases in adults are prone to be functionally suppressed by the hormone produced even by small remnants of normal thyroid gland. Thus they may not begin to show evidence of thyroid-like activity until the thyroid gland itself has been entirely extirpated. This phenomenon seems to occur less often in children, but it must be watched for carefully. Too early administration of thyroid replacement might mask the presence of otherwise undetectable but important tumor residues.

When there is no further evidence of the presence of functioning thyroid tissue and replacement medication has been started, the patient is seen at 3 month intervals, or oftener if particular circumstances seem to indicate the need. At each follow-up visit considerable attention is paid to the need for change in replacement level. A sharp decrease in the need for hormone is a warning sign of the resumption of thyroid-like activity by tumor autonomous from the TSH control mechanism. On the other hand, it is undesirable for a child to remain in the hypothyroid state for any prolonged period, for school performance may be materially affected. On each visit there is, of course, a search for palpable processes in the neck, and roentgenograms are obtained once a year. Tracer studies may be undertaken at any time physical or roentgen findings suggest the need, but are routinely carried out semiannually for the first 5 years. Since thyroid hormone desaturation is a lengthy process and one which can be unpleasant to the patient, we now make no effort to withdraw thyroid for periodic examinations, and instead administer a tracer dose of 25 to 100 μc of an isotope of iodine, depending upon the patient's size, together with a 5 to 10 unit dose of TSH. A search for foci of isotope deposition is then carried out with a scintillation probe. If recurrences develop or new lesions arise, they are dealt with in the manner outlined by precept in the case reports above.

SUMMARY AND CONCLUSIONS

1. Thyroid cancer occurs more commonly in females than in males, and has been thought to be increasing in incidence in young people. Its cause is unknown, but one of the contributing factors may be exposure of the neck to ionizing radiation in infancy, childhood or later.

2. Differentiated carcinoma is the commonest form of thyroid cancer in childhood. Mortality from thyroid cancer is approximately 15 per cent of all patients, with two-thirds dying of the differentiated carcinomas. Forty per cent of those who die of the disease do so more than 5 years after discovery. Complication due to local recurrence and direct extension is the commonest mode of death.

3. The prognosis for survival in patients with thyroid carcinoma is good, and has led to misunderstandings about the real nature of the disease.

4. General diagnostic and therapeutic approaches for various types and distributions of thyroid cancer in children are described.

5. Representative situations in management of childhood thyroid cancer are illustrated from our own clinical experience.

6. A diagnostic and therapeutic regimen for children with thyroid cancer is outlined in detail. The role of radioiodine in the management of thyroid carcinoma in children is explored at length.

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THE ROENTGEN DIAGNOSIS OF TERATOMA OF THE THYROID REGION*

A REVIEW OF THE LITERATURE

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RECENT experience in our department with 2 proved cases of teratoma of the thyroid region has stimulated interest in the entity, with particular attention directed to the roentgenographic features of these unusual neoplasms. The 2 new cases will be only briefly treated in this paper, since they are to be more completely described elsewhere.[17,24]

Teratomas of the neck in the region of the thyroid gland have been reported sporadically since the first proved case was published by Hess[7] in 1854. Approximately 90 cases have been recorded since then, almost all in newborn infants. It has been emphasized in the more recent literature that prompt surgical removal of the tumor is essential for survival if the commonly noted signs and symptoms of respiratory obstruction are present. Roentgenographically visible calcification within the tumor has been mentioned by a few authors as being a

Table I

SUMMARY OF ROENTGEN FINDINGS IN TERATOMA OF THE THYROID REGION

Case	Author	Year	Calcification in Tumor on Roentgenogram	Tracheal Deviation and/or Compression on Roentgenogram	Age	Sex
1	Bell[2]	1926	No*	—	Birth	M
2	Chapman[5]	1941	No	Yes	9 da.	M
3	Sutton and Gibbs[18]	1944	No	Yes	3 mo.	F
4	Munro and Waldapfell[10]	1944	Yes	Yes	4 wk.	M
5	White and Gosselin[21]	1952	No	Yes	Birth	M
6	McGoon[9]	1952	No	Yes	8 mo.	M
7	McGoon[9]	1952	Yes	Yes	2 wk.	M
8	Perkins and Pautler[12]	1953	No	No	6 da.	F
9	Thomas[19]	1957	Yes	—	Birth	F
10	Silberman and Mendelson[16]	1960	No	Yes	Birth	M
11	Silberman and Mendelson[16]	1960	Yes	No	Birth	F
12	Woolley and Harris[23]	1960	Yes	Yes	Birth	M
13	Dacso, Fukushima and Chick[6]	1962	No	No	Birth	F
14	Weitzner[20]	1964	No	No	3 wk.	M
15	Newstedt and Shirkey[11]	1964	No	Yes	Birth	M
16	Stone and Gudio[17]	To be published	Yes	Yes	2 wk.	F
17	Zwiren and Patterson[24]	To be published	Yes	Yes	Birth	F

* Specimen only.

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common feature of these malformations; the demonstration on roentgenograms of tracheal deviation and/or compression also is a frequent finding. In an attempt to more precisely describe the roentgenographic features of teratoma of the neck, the available English literature was reviewed, tabulating the reported roentgenographic findings in those cases in which adequate information is available (Table I).

REPORT OF CASES

Case I. A 3 year old white female child entered The Henrietta Egleston Hospital for Children because of rapid increase in size of an anterior cervical mass, which had first been noted at 2 weeks of age. Since birth, and intermittently thereafter, the infant experienced "strangling" episodes when feeding. Physical examination of the neck revealed a slightly asymmetric anterior cervical mass measuring approximately 5×9 cm. The mass was firm in consistency, presented nodular, cystic areas to palpation and moved with the larynx on swallowing. Thyroid function studies were within normal limits. Anteroposterior and lateral roentgenograms of the neck were obtained and are shown in Figure 1, *A* and *B*. Surgery was performed and cystic degeneration of the thyroid gland was found. A subtotal thyroidectomy was accomplished. On pathologic examination, the specimen was interpreted as a benign teratoma in the region of the thyroid gland. The postoperative course was uncomplicated and the child was well 1 year later.

Case II. A 3 hour old, white, female, premature infant was admitted to The Henrietta Egleston Hospital for Children as an emergency, having been delivered at another hospital where a large cervical mass was noted at birth. Because of severe respiratory distress at birth, an endotracheal tube was inserted. Physical examination revealed a 3 pound, 12

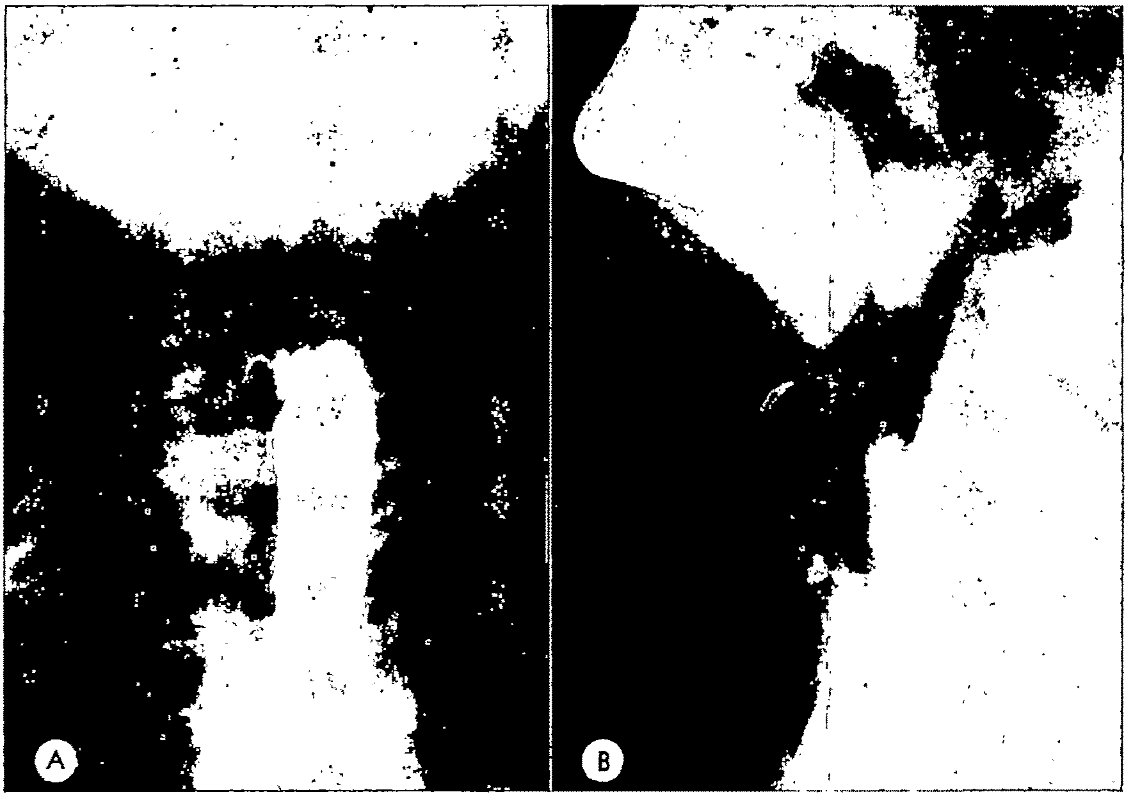

Fig. 1. Case I. (*A*) Anteroposterior and (*B*) lateral roentgenograms of the cervical area, demonstrating calcifications within a soft-tissue mass. There is slight anteroposterior compression of the trachea, as well as minimal deviation of the barium-filled cervical esophagus. The opacity in the submental area represents barium artifact.

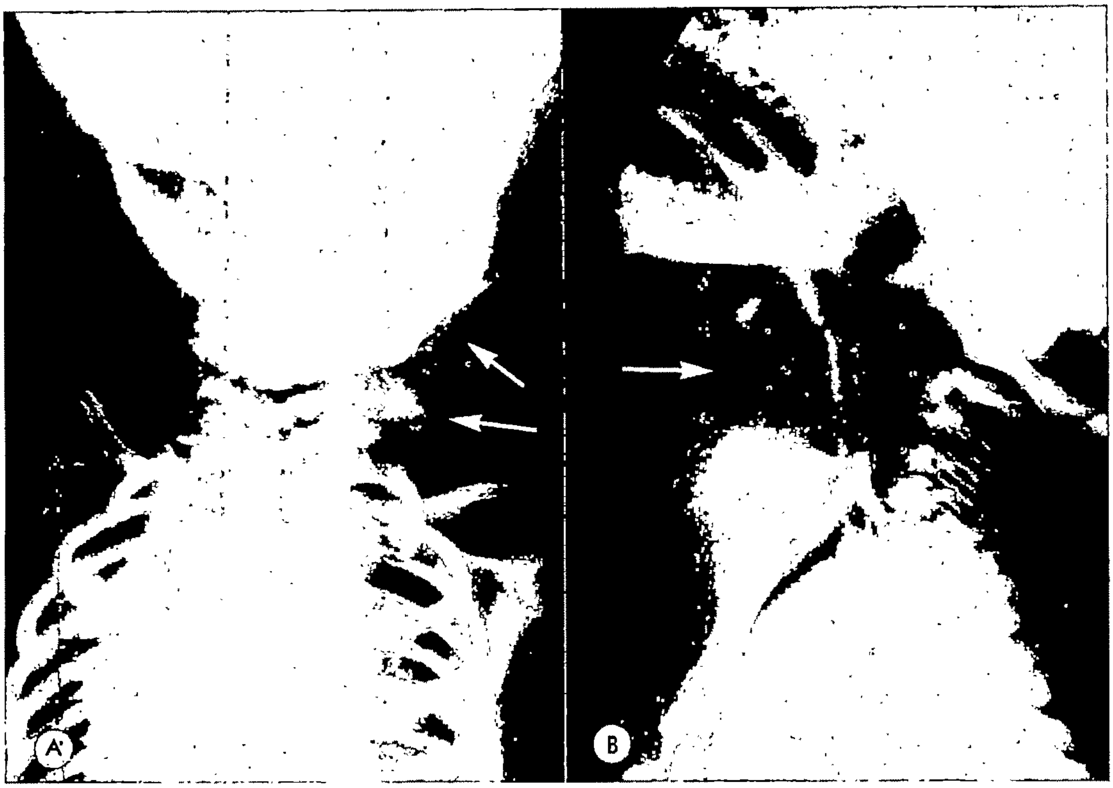

Fig. 2. Case II. (*A*) Anteroposterior and (*B*) lateral roentgenograms of the cervical area, demonstrating amorphous calcific deposits (arrows) within a predominantly left-sided soft-tissue mass. An endotracheal tube is in place. The upper trachea is displaced towards the right.

ounce infant with a multinodular, soft, cystic mass situated anteriorly but asymmetrically in the neck. Frontal and lateral roentgenograms of the thorax and neck were obtained and are shown in Figure 2, *A* and *B*. On the basis of these roentgenograms, a diagnosis of teratoma of the neck in the thyroid region was made. At surgery, a large multicystic tumor measuring 4×3×2 cm. was removed, along with several enlarged adjacent lymph nodes. Microscopic examination of the tumor showed features diagnostic of teratoma.

REVIEW OF LITERATURE IN WHICH THE ROENTGEN FINDINGS ARE DESCRIBED

Table I is a tabulation of those reported cases of teratoma of the thyroid region taken from the available English literature, and including the 2 new cases described above, in which there are descriptions of pertinent roentgenographic findings. The cases are arranged by author and year of publication. The presence of a cervical soft-tissue mass was, of course, noted in all instances, clinically and roentgenographically. In addition, the presence or absence of visible calcification in each case is recorded, as is the occurrence of tracheal compression. It should be mentioned that the teratoma reported by Bell[2] was subjected to roentgenography only after surgical removal, hence any definite information concerning its relation to the infant's trachea cannot be obtained. Of the 16 remaining cases, calcification within the tumor was identified in 7. Distortion of the trachea was apparent in 11 instances.

The soft-tissue tumor mass is most often asymmetric as seen on the frontal roentgenogram. The presence of fatty tissue in the teratoma has never been identified in the roentgenograms reported, although considerable fat is sometimes described microscopically.

The presence of calcification within the mass is the most important feature in the roentgenographic diagnosis of thyroid teratoma. Detailed descriptions of the patterns seen are lacking, the densities usually described only as multiple calcific opacities situated within the tumor. Close inspection of the original roentgenograms of the 2 cases presented above revealed the calcific deposits to assume the form of several "clusters" within the tumor mass, each cluster measuring 1–4 mm. in diameter. In a large number of cases in which roentgenograms were not obtained, both gross and microscopic bone and/or calcium deposits have been noted in the tumor specimens. It seems reasonable that in at least some of these the calcium would have been demonstrated roentgenographically had film studies been obtained.

Since, in most cases, the teratoma is asymmetrically situated in the neck, distortion of the trachea is more often apparent in the frontal than the lateral roentgenogram. However, in 1 case reviewed the trachea was observed to be deviated far anteriorly, while the esophagus was displaced posteriorly.

Silberman and Mendelson[16] describe an unusual roentgen finding in the first of 2 cases they report. In association with a predominantly left-sided teratoma, it was noted that the left half of the mandible was deformed, the normal angle between body and ramus being replaced by a straight line between the mental symphysis and the base of the skull.

DISCUSSION

OCCURRENCE

Teratomas are relatively rare in the cervical region. They arise in the following sites in decreasing order of frequency: ovary, testis, anterior mediastinum, retroperitoneal region, pineal and other intracranial locations, neck, and abdominal viscera. The branchiogenic region, particularly the thyroid area, and the sacrococcygeal region are sites of predilection for teratomas in the newborn, in contrast to the gonads in adults. Potter[13] confirms the impression that cervical teratoma, although rare, is among the tumors most frequently found in newborn infants. A number of tumors in this region was described during the seventeenth, eighteenth, and early nineteenth centuries. Many of these undoubtedly were teratomas; however, because of the lack of histologic confirmation in these early reports, they have been omitted from subsequent reviews. Ninety per cent of the recorded cases have been recognized at birth or soon afterwards. Only 4 adults with cervical teratomas have been reported. There appears to be no significant sex or racial predilection.

NOMENCLATURE

Attempts have been made in the past to distinguish between "teratoma of the thyroid gland," "teratoma of the neck in the region of the thyroid gland," and "cervical teratoma." Saphir[15] called the tumor a thyroid teratoma if the thyroid gland was absent, and a teratoma of the neck if the gland was identified.

Bale[1] advocated using both the tumor's anatomic relations and its blood supply as a means of classification. Thus, it was suggested that those tumors supplied by the superior and/or inferior thyroid arteries be designated true teratomas of the thyroid, whereas if the neoplasm were supplied by neither of these vessels but anatomically replaced the thyroid gland, not by pressure displacement but by actual absence of part or all of the thyroid, it be classified as a teratoma of the neck in the region of the thyroid. Bale further suggested that those remaining tumors not meeting either of these vascular or anatomic criteria be termed "teratomas of the neck, probably in the region of the thyroid gland."

As Silberman and Mendelson[16] have pointed out in their excellent review, this arbitrary distinction is probably invalid and has not proved very helpful. The difficulty in identifying the actual origins of the blood vessels supplying the large cervical mass is considerable; the marked displacement of anatomic landmarks in the neck, and often the absence of any recognizable thyroid tissue or thyroid arteries contribute to the problem. Thus, it has been more recently proposed that these tumors be designated simply as cervical teratomas unless the mass obviously arises from recognizable thyroid tissue, in which case it should be called a true teratoma of the thyroid gland.

PATHOLOGY

The term teratoma comprises certain true tumors and progressively growing tumor-like embryonal inclusions, in which representative tissues of all three embryonal layers are present in disorderly fashion. Willis[22] defines a teratoma as a neoplasm composed of multiple tissues foreign to the part in which it arises, both in benign and malignant forms.

Cervical teratomas are almost always benign, true neoplasms composed of varying portions of the primordial germinal layers. Although they are basically solid tumors, progressive accumulation of secretions of the epithelial components may result in a predominantly cystic lesion. The frequent recognition of neural tissue in the microscopic sections has been mentioned by several authors in the past. This finding has been recorded in almost 80 per cent of reported cases, but should not be considered unusual or characteristic since it has been observed in an equally high proportion of all teratomas.

While the great majority of these neoplasms have been interpreted as benign on histologic examination, few long-term follow-ups have been recorded. Four definite cases of malignancy have been reported to date; 3 of these have been in adults. There has been only 1 well documented instance of malignancy in an infant, that described by Pupovac.[14]

SIGNS, SYMPTOMS, AND DIAGNOSIS

Frequently recorded in the literature is the presence of hydramnios in cases of cervical teratoma. This observation coincides well with the high incidence of hydramnios which is known to occur in cases of fetal malformation in general. Depending upon the size of the tumor, it may also cause hyperextension of the neck and result in malpresentation of the fetus and dystocia.

Teratoma of the neck almost invariably presents as a mass in the neck of a newborn infant. The tumor is usually large, bulky and asymmetric, occupying most, if not all, of the thyroid region. It may extend from the mastoid process and the angle of the mandible superiorly to the clavicle below, and may occasionally extend inferiorly to involve the retrosternal area. Palpation reveals a partially firm, solid tumor with numerous cystic areas within its irregular, lobulated surface. The teratoma usually presents rather well-defined borders and is at least partially movable both over the deeper tissues and beneath the skin.

Of the cases reported which were not stillborn, the great majority presented acute symptoms at birth. These included cyanosis, dyspnea, apnea, and stridor secondary to tracheal compression. In a few instances, difficulties of swallowing were observed. The degree of respiratory obstruction may be so severe that the infant dies soon after birth unless surgical removal of the offending mass is accomplished. Occasionally, the infant may be asymptomatic at birth, only to develop features of airway obstruction several weeks or months later. Rarely, the tumor may remain entirely asymptomatic.

While the chief tumors which require differentiation from teratoma are cystic hygroma, branchial cleft cyst, and congenital goiter, a more complete differential diagnosis for the clinician includes simple multilocular cyst, dermoid cyst, parotid gland tumor, thyroglossal duct cyst, lymphangioma, thyroid carcinoma, and neuroblastoma. In Buckwalter and Layton's[3] case of malignant teratoma in an adult, carcinoma of the thyroid gland was considered.

ROENTGEN FEATURES

The essential roentgen features of thyroid teratoma in infants and children include:

1. The demonstration of a soft tissue mass in the neck. This is usually asymmetric and may occasionally produce some degree of extension of the neck.
2. Distortion of the trachea. This has been noted in considerably more than half the cases reviewed.
3. The presence of calcification within the tumor mass. This is the most important characteristic finding. Most often, one or more small clusters of calcium may be demonstrated within the mass. Since this feature is almost diagnostic, considerable care should be used in examining the roentgenograms.

ROENTGEN DIFFERENTIAL DIAGNOSIS

The roentgen differential diagnosis depends on whether or not there is calcification visible within the cervical mass. If not, congenital goiter, cystic hygroma, and lymphangioma are good possibilities. The presence of a thyroglossal duct cyst should also be considered, but this tends to be small and situated in the midline. Tumors of any of the soft tissues of the neck such as angiomas of the strap muscles may produce masses similar to cervical teratomas. Other possible diagnoses if the mass presents no visible calcium are listed above. If there is calcification within the mass as demonstrated on the roentgenogram, the presence of a teratoma is almost certain. As far as can be ascertained from the literature, calcium has not been identified in roentgenograms of any of the other diagnostic possibilities, at least not in the newborn or young infant.

Care should be taken to distinguish physiologic calcification in the anterior cervical area from that occurring in a teratoma. Thus, ossification of the hyoid bone, which begins during the fourth and fifth months of pre-natal life, was visible in roentgenograms of 60 to 75 per cent of normal newly born infants examined by several authors, quoted by Caffey.[4] However, the developing ossification centers of the hyoid bone present smoother, more regular outlines on the lateral roentgenogram of the neck than do the pathologic calcifications found in teratomas. Likewise, physiologic or premature ossification of the temporal bone's styloid process and stylohyoid ligament, as well as the laryngeal cartilages, may temporarily be a source of confusion.

Calcifying tuberculosis of the cervical lymph nodes could conceivably be confused with the roentgen features of teratoma, but the age of the child and the presence of a much larger, cystic cervical mass in the latter condition should be sufficient to quickly distinguish these.

TREATMENT AND PROGNOSIS

The most important principle in the treatment of cervical teratoma in infants is prompt operation, particularly when symptoms of tracheal and esophageal obstruction are present. It should be emphasized that no infant exhibiting such obstructive symptoms has survived unless surgical removal was performed. Preoperative measures include tracheal aspiration, oxygen therapy, and, often, tracheal intubation. Only occasionally has preoperative tracheostomy proved helpful; in the majority of the cases in which this procedure has been attempted, the large size of the tumor has prevented adequate exposure of the trachea and the infants have died of anoxia.

Because of the undesirable sequelae of hypothyroidism in infancy, a few of the more recent articles advocate the administration of thyroid extract supplements postoperatively until it is possible to show that endogenous thyroid function is present.

From a review of cases in the literature, approximately 16 per cent of babies with this tumor have been stillborn. Of those born alive and who were operated, about 90 per cent survived. On the other hand, all patients not treated surgically died.

SUMMARY

The presence of a cervical mass in an infant or young child should lead the clinician and roentgenologist to suspect the entity of teratoma of the thyroid region. In addition to briefly presenting 2 new cases, the available English literature was reviewed, tabulating the roentgen findings of those reported cases in which film interpretations were available. Demonstration of calcification within the tumor, when present, is virtually diagnostic of cervical teratoma, having been identified in about 40 per cent of the cases. Distortion of the tracheal air column on the roentgenogram is an even more frequent sign but is much less specific. The roentgen differential diagnosis is presented.

In a general discussion of cervical teratomas, the occurrence, nomenclature, pathologic findings, clinical features, treatment, and prognosis are reviewed. The importance of accurate and early diagnosis is stressed, since failure to surgically remove the teratoma leads to progressive respiratory embarrassment and death.

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UNUSUAL FACIAL TUMORS IN THE NEWBORN*

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SIX unusual cases of tumors in the newborn have been found in a review of the records of the Children's Hospital Medical Center of the past 25 years. Two are instances of what we believe to be a previously undescribed "adenocarcinoma" of the parotid gland in this age group and therefore a distinct pathologic entity, and 4 are cases of "teratoma" about the face.

Carcinoma arising in the region of the parotid and salivary glands is a most unusual finding in childhood. Of those recorded in the literature, undifferentiated carcinomas comprise approximately 20 per cent,[6] only 1 instance of which occurred in the neonatal age group.[4] Well differentiated adenocarcinoma in this site, in the neonate, has not obviously been recorded in the literature. Howard *et al.*[5] have reported 2 cases in somewhat older children of what we believe to be a more undifferentiated carcinoma than the cases included in this report.

Teratomas on or near the face in the newborn are also unusual. Ariel and Pack[2] described teratomas in the cheek and floor of the mouth as atypically located but gave no specific reference to such. Indeed, Ariel and Pack noted that teratomas of the neck generally are among the rarer tumors and reported that there are only approximately 75 cases in all in the world medical literature.

REPORT OF CASES

CASE I. M.M. This female child, a product of normal pregnancy and delivery, was found at birth to have a mass in the region of the left parotid gland. On the sixth day of life, a biopsy specimen at another hospital was diagnosed as adenocarcinoma of the parotid gland. She was admitted to the Children's Hospital Medical Center at the age of 10 days. She was found to have a firm mass, measuring 5×6 cm., which involved the left parotid gland, extended an indefinite distance into the deep tissues of the face, elevated the left ear, and impinged on the ear canal and the anterior margin of the left ear (Fig. 1).

Roentgenograms demonstrated a large soft tissue mass extending outward from the left parotid area; the left hemi-mandible was completely absent. No calcifications were seen within the mass (Fig. 2, *A* and *B*).

Shortly after her admission, the mass was explored surgically. It was found to have extended by means of a stalk into the region of the maxillary bone and sinuses; it penetrated deeply into these structures and could not be excised. Approximately only 90 per cent of the mass was therefore removed.

On histologic examination the tumor was found to be partly encapsulated by fibrous tissue and smooth muscle; normal serous-type salivary gland tissue could be distinguished around the tumor. The tumor itself was uniform in appearance and composed of rounded masses separated by connective tissue bundles. The lobules were composed of large polyhedral cells with well defined cell membranes. Mitoses were frequent (Fig. 3). A diagnosis of adenocarcinoma of the parotid gland was made.

Following partial excision, irradiation (2,600 r in 29 elapsed days to the midplane of the left parotid; factors: 250 kv.p., 15 ma., Thoraeus 2 filter, half value layer 2.6 mm. Cu) and chemotherapy were instituted; she has remained free of disease for the past 3 years.

CASE II. J.J. This male child, a product of a normal pregnancy and delivery, was found at birth to have a mass overlying the right cheek, just anterior to the right ear. On admission to the Children's Hospital Medical Center, at 1 day of age, the mass, which measured 5×5 cm., was found to be firm and covered by skin which was bluish, thin, shiny and atrophic; there were dilated veins over this area. The mass was freely movable over the mandible; it appeared to be in the right parotid gland and not attached to deep structures, although it was fixed to the overlying skin (Fig. 4).

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Roentgenograms demonstrated a large soft tissue mass extrinsic to the right hemi-mandible, although there appeared to be slight erosion of the cortex of the mandible at one point. Within the periphery of the mass was a thin shell of calcification (Fig. 5).

The tumor was excised although it had extended into the pterygoid fossa. Histologic examination revealed solid masses of epithelial cells, the latter separated by scanty connective tissue. These masses of epithelial cells were surrounded by dense fibrous stroma. No mitoses were seen. Several small ducts and small groups of cells with definite acinar arrangement were in the tumor. Areas of infarction, hemorrhage, and necrosis were noted. Compressed parotid remnants were found outside the mass (Fig. 6). A diagnosis of adenocarcinoma of the parotid gland was made.

Following excision and irradiation (2,200 r in 14 elapsed days delivered to the midplane of the right parotid; factors: 200 kv.p., 10 ma., 0.5 mm. Cu+1 mm. Al filter, half value layer 1.25 mm. Cu), he was readmitted twice within the year for treatment of local recurrences. After the third excision at the end of the first year, he remained free of disease during the next 12 years, up to the present time.

Case iii. R.B. This female child, a product of a normal pregnancy and delivery, was found at birth to have a mass in the region of the right jaw. She was admitted to the Children's Hospital Medical Center when 6 days old with a large mass measuring 5×5 cm. in the area of the right mandible. The mass was soft and fluctuant on palpation and it transilluminated. It did not appear to be fixed. It extended from the mandibular fossa to the point of the chin, upward approximately halfway to the eye, and downward almost to the cricoid cartilage. Internally, it pushed the mucosa inward and elevated and medially displaced the lower gum (Fig. 7).

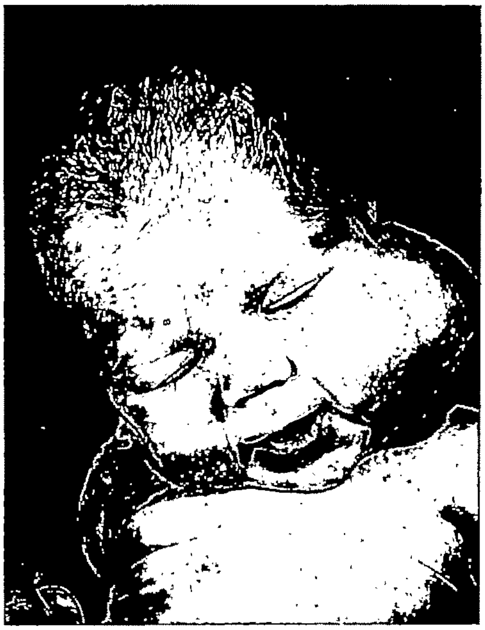

Fig. 1. Case 1. Mass involving left parotid gland, measuring 5×6 cm.

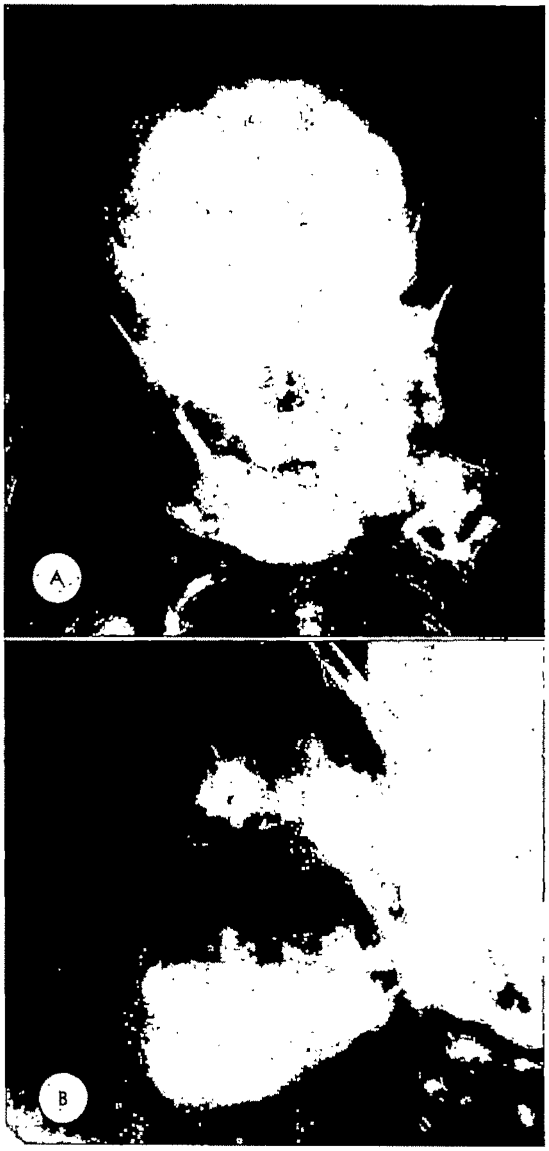

Fig. 2. Case 1. (*A* and *B*) Anteroposterior and left lateral roentgenograms showing the parotid mass and the absent left hemi-mandible.

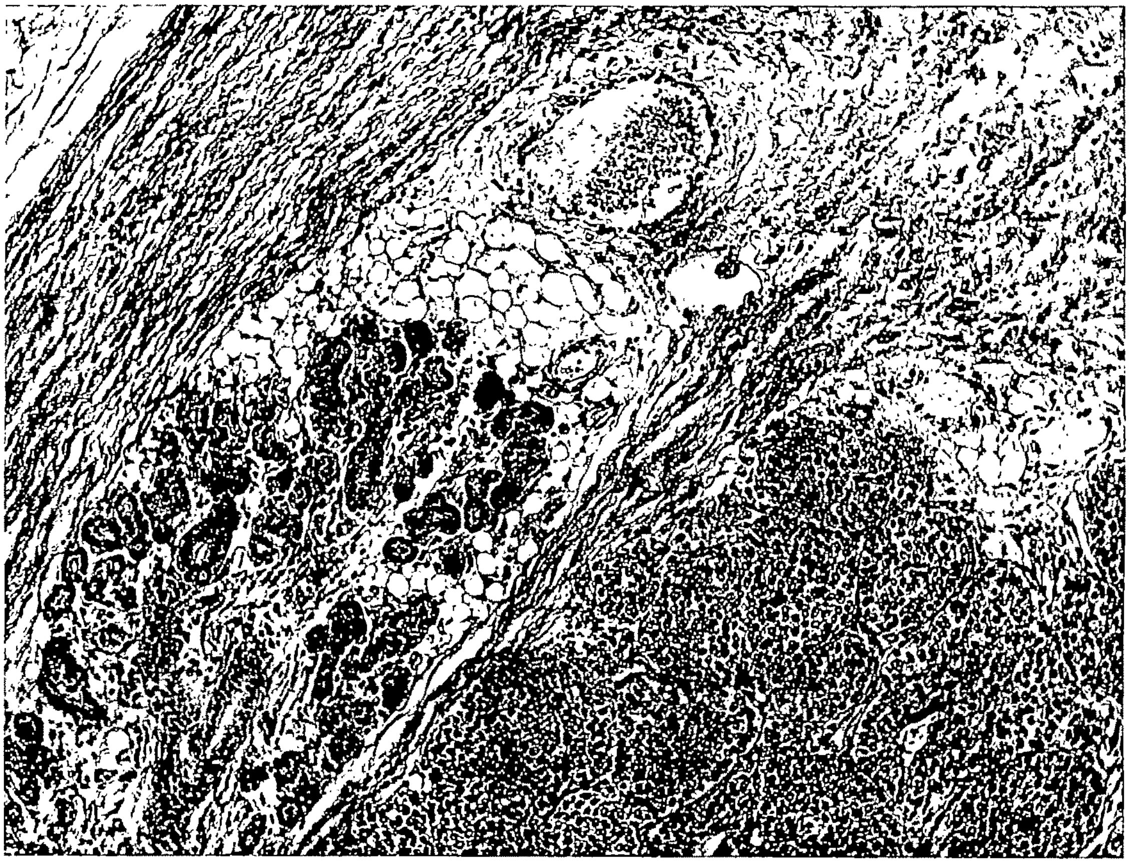

Fig. 3. Case i. Solid masses of tumor are separated from normal immature parotid gland by a thin fibrous septum (×140).

Roentgenograms demonstrated a large soft tissue mass which was lobulated and in which there were dense calcifications or actual bone. There was considerable abnormality of contour of the right ramus of the mandible with a small spur anteriorly and a large exostosis on the inferior aspect of the horizontal part. No gross destruction of the mandible could be detected although minor erosion could not be excluded (Fig. 8, *A* and *B*).

The subcutaneous tissues were found to be free of apparent infiltration by the mass which peeled away readily. The mass apparently was removed *in toto*.

Histologic sections revealed large areas of nerve tissue which in part were covered by a single layer of columnar epithelium. Lobulated glandular tissue was also noted; it was partly mucous and partly serous and had large ducts lined by cuboidal epithelium. Several sections showed villous-like projections of epithelium into a cavity, resembling in appearance choroid plexus or a fallopian tube. Cells suggestive of ganglion cells were also seen; these were large cells with round to oval, pale but granular nuclei, prominent nucleoli, and very granular cytoplasm. The stroma was composed of irregular bands of fibrous tissue interspersed with vessels and aggregations of nerve or glandular tissue. A diagnosis of teratoma was made.

She has remained well to the present time.

Case iv. E.G. This child, a product of a normal pregnancy and delivery was admitted to the Children's Hospital Medical Center at the age of 1 day with a large mass in the region of the right jaw. The 3×5 cm. mass was soft and lobulated and the overlying skin was erythematous and tense. The mass was just anterior to the right ear, below the zygoma, and extended to the anterior corner of the mouth. Superiorly, it displaced the right maxilla upward and continued intraorally to partially fill the nasopharynx and also cause downward displacement of the palate. Inferiorly, it extended 4 cm. below the margin of the mandible.

Roentgenograms demonstrated a mass situated superficially to the right mandible, with erosion of the posterior half of the right mandible. No calcification could be seen within the mass (Fig. 9).

Following incomplete excision of the mass, histologic examination revealed disorganized brain tissue, composed primarily of neuroglia, with many oligodendroglia and astrocytes. An occasional neurone was seen. Small canals lined by ependyma were noted and, in one of the larger canals, an infolding of the ependyma formed a small segment of choroid plexus. No mitoses were noted.

The child died within the next year owing to local extension of the tumor.

Case v. S.C. This female child, a product of a pregnancy complicated by polyhydramnios and ruptured membranes, entered the hospital when 7 days old with a mass on the left side of the face. The mass was soft and measured 5×4 cm. Its posterior margin was just anterior to the left mastoid process and it had caused subluxation of the left temporo-mandibular joint. Medially, it extended to the midline. It extended into the mouth where it filled the left vestibule and caused marked depression of the uvula and soft palate.

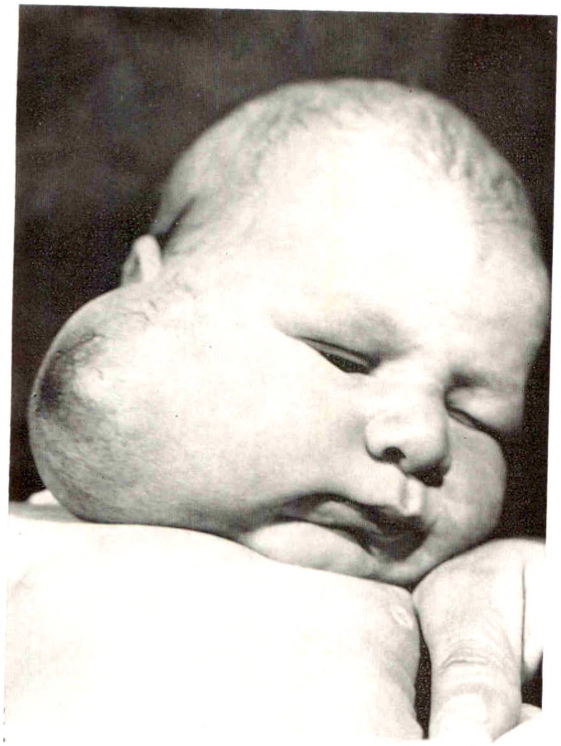

Fig. 4. Case ii. Mass measuring 5×5 cm. involving right parotid gland. Note discolored overlying skin.

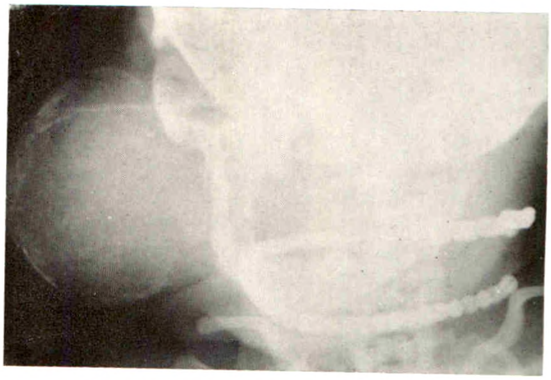

Fig. 5. Case ii. Mass with peripheral calcification in the right parotid. There is slight erosion of the external surface of the right hemi-mandible just under the lesion.

Roentgenograms demonstrated a large soft tissue mass, extrinsic to the left mandible with distortion of the mandible owing to its expansion but with no obvious bone erosion. No calcification could be seen within the mass (Fig 10).

Microscopic examination, following excision of the bulk of the mass, revealed mainly glial elements, chiefly astrocytes. Areas suggestive of meninges, neurones and ependymal-lined clefts with immature choroid plexus tissue were noted (Fig. 11). A diagnosis of teratoma was made.

During the next year, local regrowth and metastases to the lungs occurred. Biopsy specimens during this period revealed malignant teratoma or embryonal carcinoma. At this time roentgenograms demonstrated destruction of the mandible near the primary tumor and the histologic sections showed epithelial tumor cells with large clear nuclei and abundant cytoplasm. Fairly well developed salivary gland tissue was present in 2 of the histologic sections. There was abundant mesenchymatous tissue as well as mucoid tissue.

Despite radiation therapy, chemotherapy, and local excision, the patient died from metastatic spread to lung and bone approximately 2 years after the diagnosis was first made.

Case vi. B.G.P. This female child, a product of a normal pregnancy and delivery, was ad-

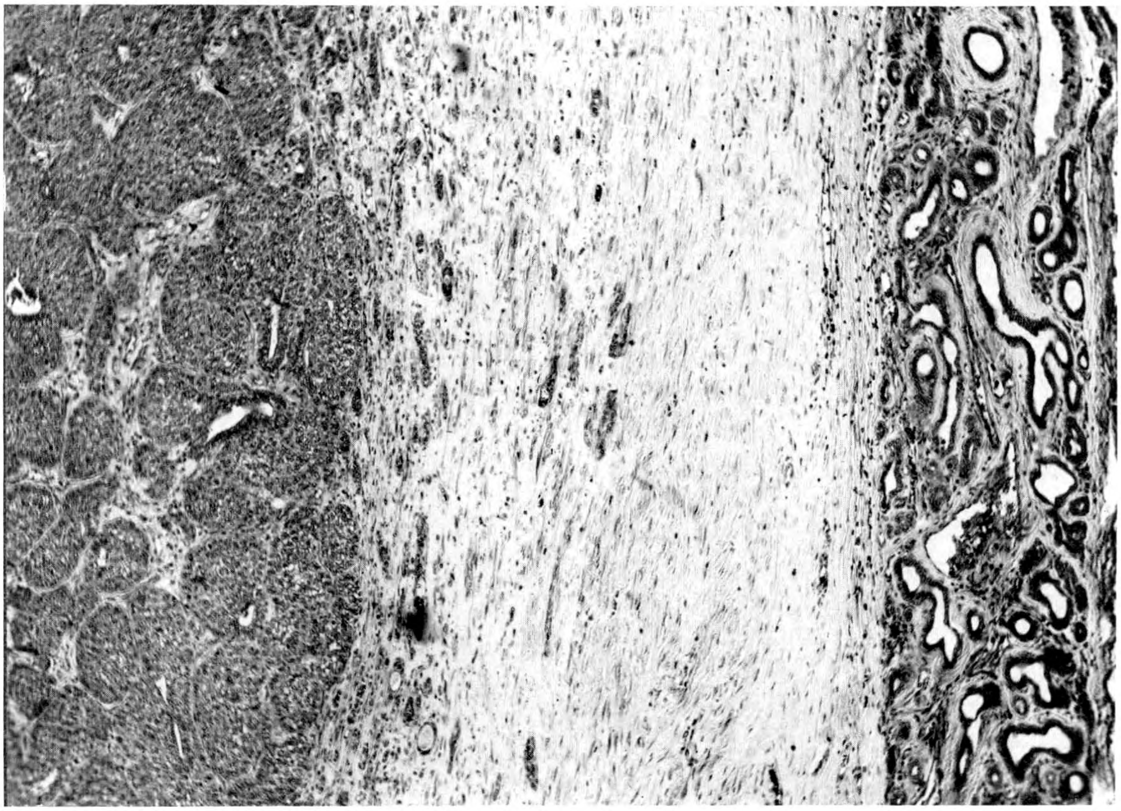

FIG. 6. Case II. Tumor on the left is separated from salivary gland on the right, which shows obstruction atrophy, by a broad zone of connective tissue (×94).

mitted, when 5 days old, to the Children's Medical Center with a mass over the left face. The mass was 14×8 cm. in size and was covered by freely movable skin (Fig. 12). The mass was bone-hard to palpation and had cyst-like areas within it. The left orbital ridge and maxilla flared out into the tumor margin. Bulging inward, the mass pushed the left buccal mucosa between the gums. The left half of the arch of the mouth was pushed to the midline, causing an unusually high arch; this deformity was believed to be the cause of poor sucking by the infant.

Roentgenograms demonstrated elevation of the infra-lateral margin of the left orbit with possible destruction of the left zygomatic arch. There was a large amount of amorphous calcification throughout the lesion which made study of the underlying facial bones difficult (Fig. 13, *A* and *B*).

On excision, examination revealed many cyst-like structures, most of which contained clear fluid. The cystic structures were lined by stratified ciliated columnar epithelium which in some areas became double layers of ciliated transitional cells. Numerous rounded, small, compound racemous glands were noted in adjacent regions of the cyst. The cells comprised dark staining nuclei with granular cytoplasm. Other regions contained stratified squamous epithelium within large round rete pegs. There were many neurofibers and much glial tissue throughout. One section contained well-defined cerebellar tissue and a fragment of osseous tissue within the mass. In addition, there were well-defined muscle bundles and heavy deposits of fat. Numerous hair follicles, sebaceous glands and sweat glands were noted in a region of corium and epidermis (Fig. 14). A diagnosis of teratoma was made.

DISCUSSION

The 6 patients here reported were similar, at presentation, with respect to age, anatomic locality, and, to some extent, roentgenographic features.

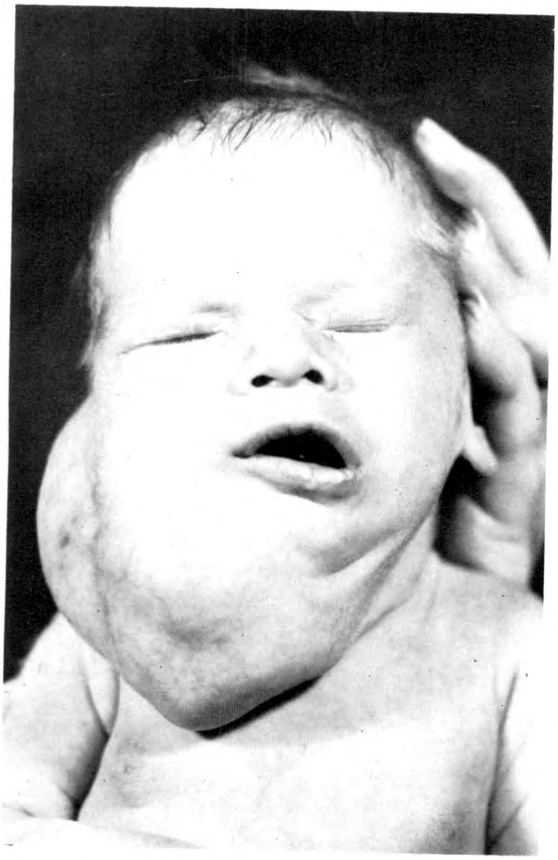

Fig. 7. Case III. Large mass lesion extending from just below the right orbit and almost to the cricoid cartilage. Its origin seemed to be about the area of the right mandibular fossa.

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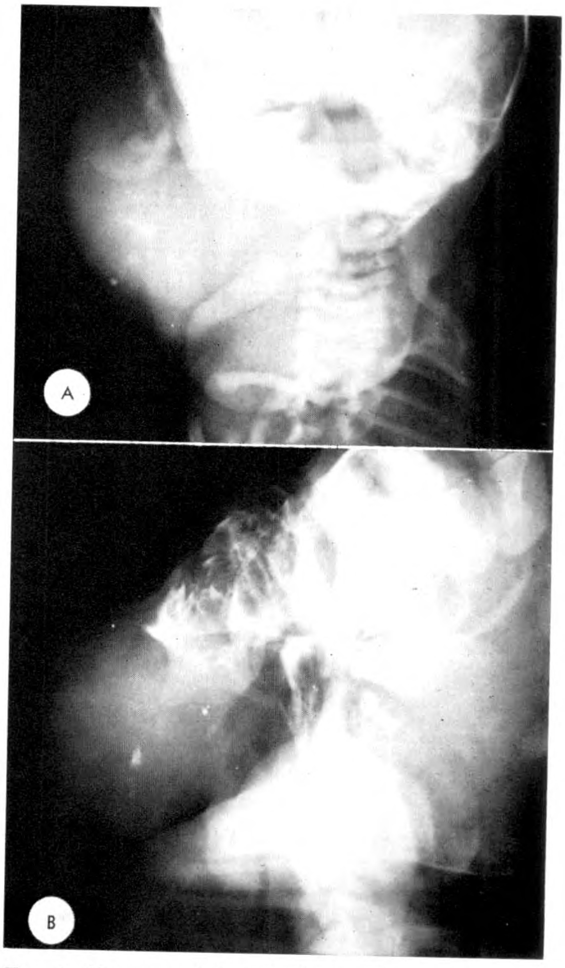

Fig. 8. Case III. (*A* and *B*) Anteroposterior and right lateral roentgenograms showing a soft tissue mass over the right facial area with intrinsic radiopacities. The exostosis can be seen in the lateral view.

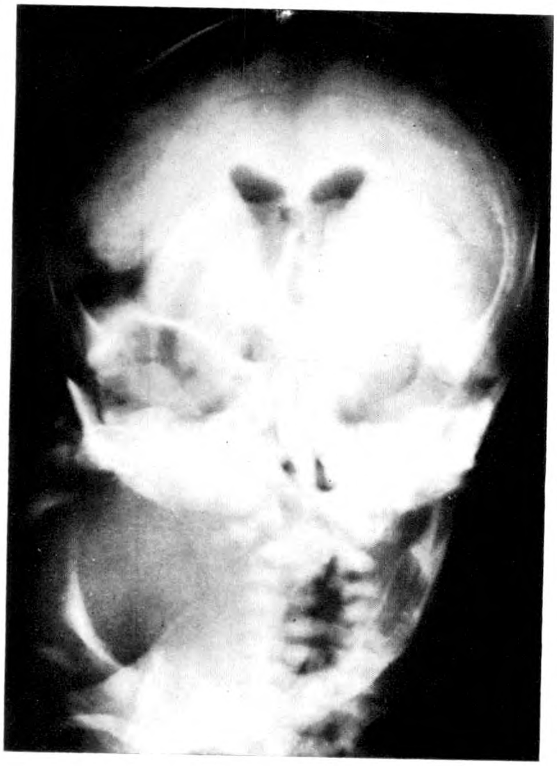

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Fig. 9. Case IV. Expansion of the right mandible with erosion of its posterior aspect.

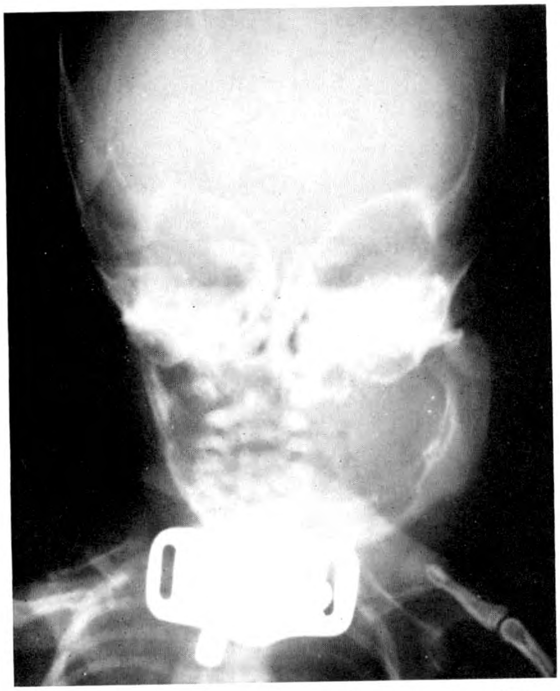

FIG. 10. Case v. Expansion of the left mandible can be seen. No destruction was noted.

All the tumors were noted at birth and can therefore be classified as congenital. They all presented as masses of approximately the same clinical appearance, located in the region of the facial bones. The degree of involvement of deep structures seemed to be somewhat greater in the 4 latter patients, 2 of the 4 showing nasopharyngeal involvement and palate depression. Clinically, the more localized lesions in Cases I and II might be considered consistent with a localized and well differentiated malignant tumor of the parotid gland, although, at operation, extension into the maxillary sinus was noted in Case I and into the pterygoid fossa in Case II.

On roentgenographic examination, all showed a soft tissue mass extrinsic to the facial bones, and, except Case v, involvement of the facial bones at the site of the main mass. However, Case v did show facial bone destruction when the tumor re-

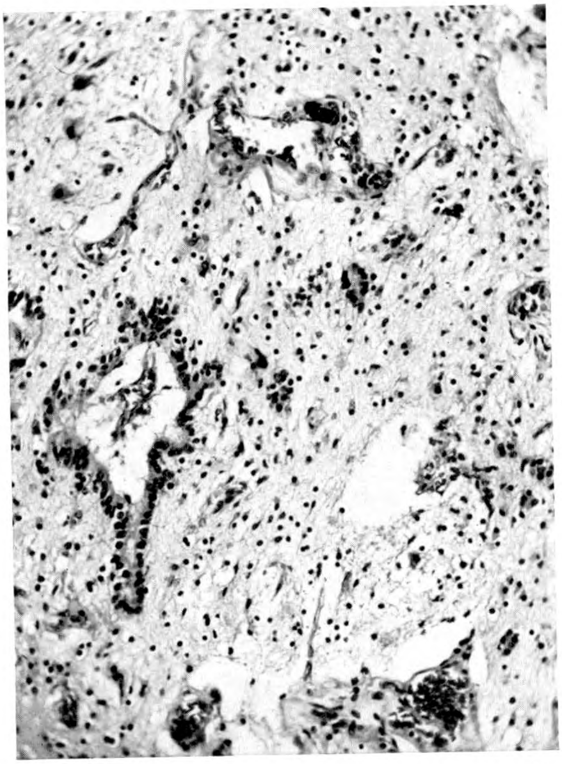

FIG. 11. Case v. An area from the teratoma containing central nervous system tissues and epithelial-like spaces, possibly ependymal (×141).

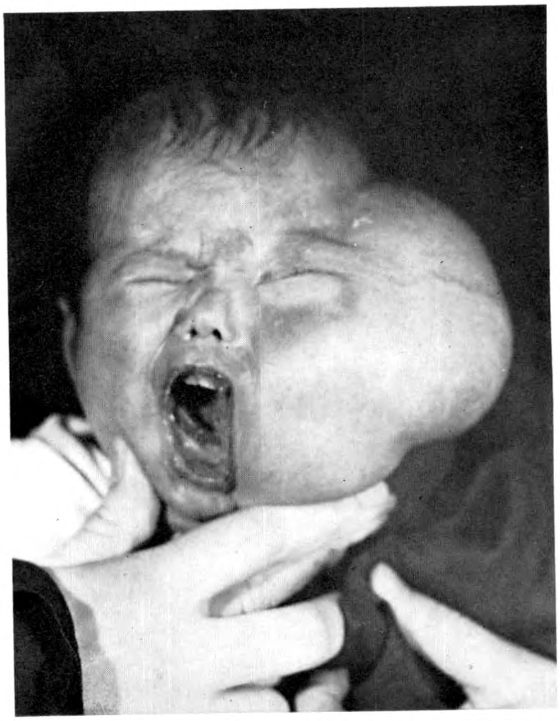

FIG. 12. Case VI. Large mass over the left face extending from the left orbital ridge to the left mandible.

curred. The degree of bone involvement ranged from expansion of the facial bones without obvious destruction (Case V), through cortical destruction in one small area (Case II), to total absence of a hemimandible (Case I).

The calcification ordinarily associated with teratoma was found in only 3 patients, 1 of whom had an "adenocarcinoma" (Case II). Two teratomas (Cases III and VI) showed calcification and probable bone production. It should be noted that the calcification in Case II might well have been due to the necrosis and hemorrhage seen on the histologic sections.

It is possible that all 6 patients represent examples of teratomas which arose in the region of the base of the brain and that the tumors in Cases I and II were of ectodermal origin with epithelial differentiation. However, we believe that these first 2 cases of "adenocarcinoma" may comprise a distinct pathologic entity and may not be teratomas of ectodermal origin. Indeed, neoplasms in these 2 patients may have been of parotid origin and similar to the rare cases reported by Ackerman and del Regato[1] as "adenoma of the salivary gland" in the adult. If they are not of this type, they have no exact counterpart in the adult literature. They are obviously not similar to the mucoid epidermoid or mixed tumor of the parotid gland.

The remaining 4 cases are best classified as epignathi and teratomas of the base of the skull.[8] Tumors of this type should be attached to the roof of the pharynx or palate and should project into the mouth as nasal cavities as they did in Cases III through VI. If this diagnosis is valid the survival of Cases III and V is unusual.[8] It should be emphasized that these tumors are different from the teratomas of the neck that arise in or near the thyroid gland.[3,7,8] Also the records of the Children's Hospital Medical Center contained no instance of hemangioma in the facial area, more specifically in the parotid gland, that showed the clinical features described above.

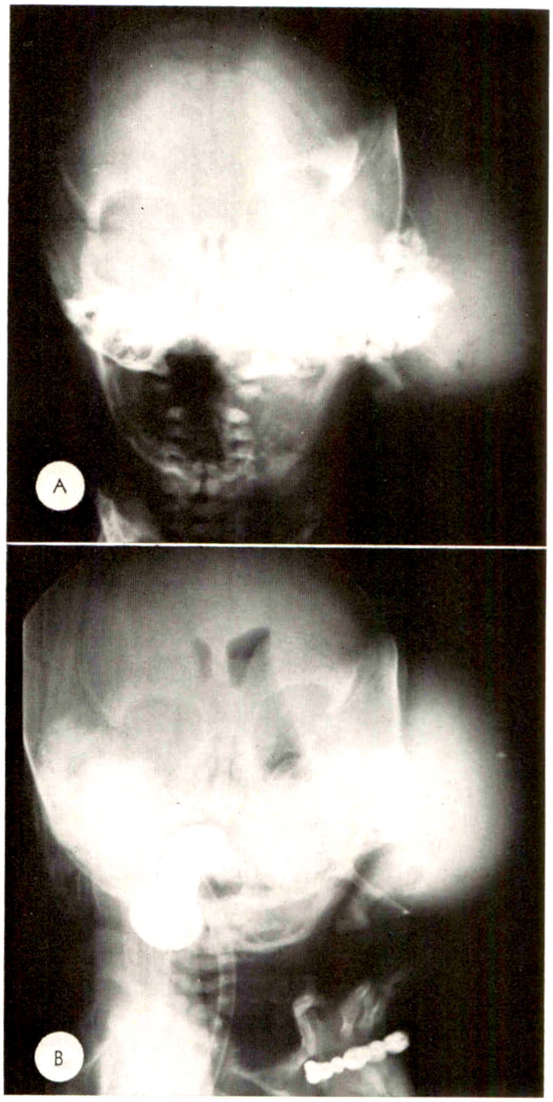

FIG. 13. Case VI. (*A* and *B*) Anteroposterior roentgenograms showing the large soft tissue mass within which is dense calcification.

SUMMARY

Six patients, in the newborn age group, with unusual facial tumors are reported; 2 of the tumors were well differentiated adenocarcinomas of the parotid gland and 4 were teratomas in the facial area.

There were many points of similarity among all 6, both in clinical and roentgenographic findings. However, the two types of lesions were different on histologic examination and hence probably are distinct pathologic entities. A more complete

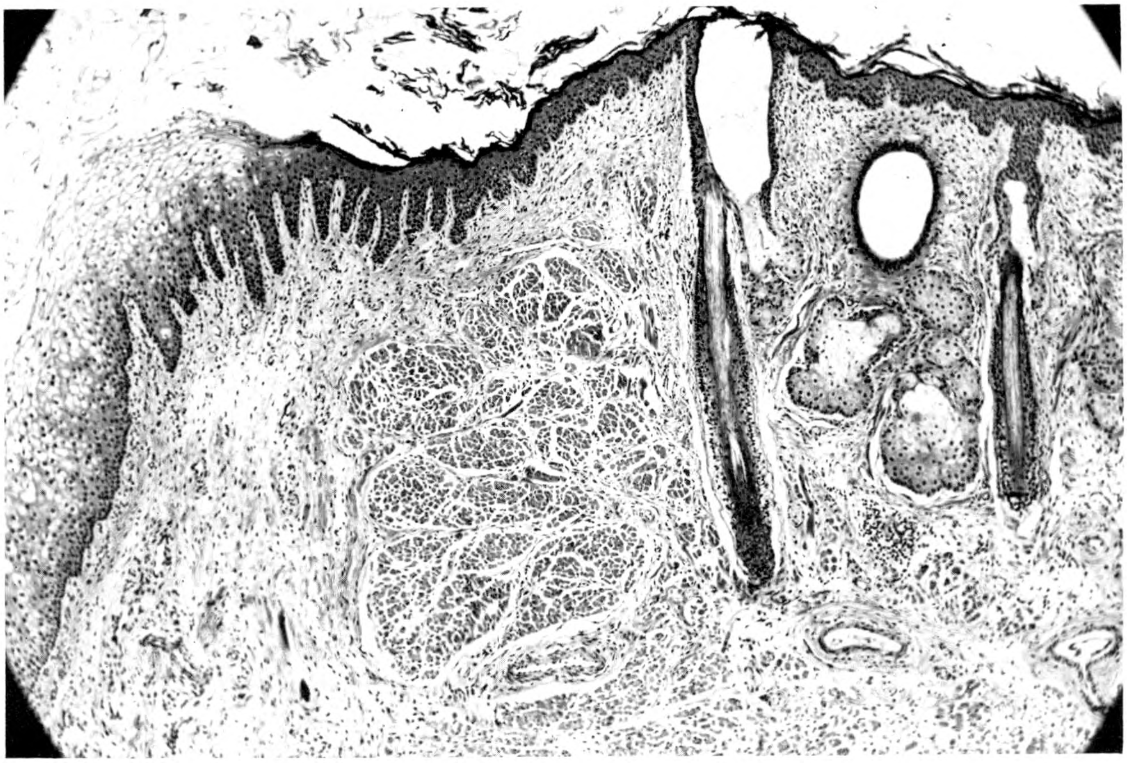

FIG. 14. Case VI. This portion of the wall of a cystic area of teratoma demonstrates a muco-cutaneous junction with abnormal admixtures of skeletal muscle beneath (×70).

description of the unusual adenocarcinoma of the parotid gland in the newborn will be presented by one of us (G. V.) in another communication.

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We wish to thank Dr. James Potchen for his help in gathering some of the material.

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ROENTGEN FINDINGS OF INCREASED INTRACRANIAL PRESSURE AND COMMUNICATING HYDROCEPHALUS AS INSIDIOUS MANIFESTATIONS OF CHRONIC HISTIOCYTOSIS-X*

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TO REPORT a new roentgen finding in the broad spectrum pathologically included under the term histiocytosis-X would not be expected to create a tidal wave of medical interest. In spite of this, additional information facilitates the correlation of the unexpected with the expected manifestations of the disease, thereby eliminating lengthy investigations.

This report deals with roentgen and clinical evidence of increased intracranial pressure associated with communicating hydrocephalus in children with histiocytosis-X of the chronic type. No attempt is made to review all facets of the multifaceted disease. Unfortunately, finding yet another manifestation of histiocytosis-X does not solve the unknown causal relationship of this disease, but it has prompted Dr. M. Nesbit and his associates of The University of Minnesota Department of Pediatrics to develop a new approach to therapy. This will be reported elsewhere.

One of us (S. B. F.) has been interested in the acute and subacute forms since the observation and subsequent study of the gastrointestinal and mesenteric manifestations of reticuloendotheliosis of the histiocytosis-X type.[4] At that time 22 cases, current and old, pediatric and adult, were reviewed at The University of Minnesota Hospitals.

In contrast to the previously reported acute and subacute cases in which nonspecific vomiting and diarrhea were described, the case findings to be described here are those of insidiously developing increased intracranial pressure and communicating hydrocephalus. The current cases under observation and the old ones found by reviewing their records and their roentgenograms retrospectively were all in the chronic stages of the disease.

MATERIAL

In April, 1963, when one of the chronic cases of histiocytosis-X followed at The University of Minnesota Hospitals since 1960 was observed to have clinical and roentgen findings of increased intracranial pressure, studies were undertaken to determine its relationship to the patient's known disease and to determine whether this was an isolated finding.

During 1963 and at the turn of the 1963–1964 calendar year, 4 cases of histiocytosis-X were found to have increased intracranial pressure. An interesting associated finding in 2 of these cases, when their records were reviewed, was that of obvious gastrointestinal involvement. During their acute and subacute phases, diarrhea and vomiting were the causes of concern. Unfortunately, barium studies were not performed when the symptoms were a clinical problem.

Only 4 current cases which had air and angiographic examinations are summarized. The results of a study of 41 cases from the University of Minnesota Hospitals are also summarized and presented in table form (Table 1).

REPORT OF CASES

CASE 1. K.A., a 6½ year old female, had multiple admissions to the University of Minnesota Hospitals with a history of many infections since the age of 1. When seen for the first time in

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TABLE I

CRANIAL AND INTRACRANIAL ROENTGEN FINDINGS IN 41 CASES OF HISTIOCYTOSIS-X AT THE UNIVERSITY OF MINNESOTA HOSPITALS

Suture spreading	2
Suture spreading and communicating hydrocephalus on air studies	4
Suspicion of suture spreading	2
Histiocytosis skull findings without roentgen evidence of increased pressure	8
Completely negative skull roentgenograms	7
Various stages of central nervous system postmortem findings without roentgen studies or roentgen evidence of increased pressure pre mortem	10
Negative central nervous system postmortem findings	4
No skull roentgenograms of postmortem studies made	4
	41

1960, right proptosis, irritability, and failure to thrive were the findings. Diabetes insipidus, lymphadenopathy, hepatomegaly, and seborrhea were recorded in March, 1961. Proptosis increased by April, 1963, at which time bilateral papilledema of 2–3 dipoters elevation of the blurred disks was found. Tooth decay and gingival changes were obvious. Hepatomegaly increased. Deep tendon reflexes were active on the left.

Laboratory studies were numerous in number and type. The positive findings were limited to inability to concentrate urine. Liver scan with rose bengal I^{131} showed three pale areas suspicious for cirrhosis confirmed by biopsy. The alkaline phosphatase was elevated.

Roentgenographic examination showed multiple zones of bone destruction typical for histiocytosis-X. In addition, cranial suture separation was obvious in April, 1963. Air studies showed communicating hydrocephalus (Fig. 1, *A-C*). In spite of extensive temporal bone involvement, no evidence of dural sinus invasion and/or obstruction was found on angiography (Fig. 2, *A* and *B*). Biopsy of the meninges and cortex was normal.

Therapy included irradiation, steroids, velban, mustards, methotrexate, and pitressin.

CASE II. A.L. is a 6 year old female. Diarrhea, lethargy, fever, rash and irritability were the initial findings as early as the first week of life in 1959. By the time her increased intracranial pressure was studied in August, 1963, she had 14 University of Minnesota Hospitals admissions. In all she had most systems involved and symptoms therefrom. She had prominent exophthalmus but no evidence of diabetes insipidus. In addition she had obvious steroid induced Cushingoid findings and chemotherapeutically induced stomatitis.

In September, 1960, papilledema was recorded by one observer but no further note was made of it until August, 1963, when she was seen for neck pain, headache, and irritability which led to the "rediscovery" of papilledema and suture spreading (Fig. 3, *A-C*).

Her multiple laboratory studies were essentially normal. The alkaline phosphatase was elevated. The N. I. H. isolated the same cytotoxic agent as obtained from eosinophilic granulomas and Hand-Schüller-Christian disease.

Her composite extensive roentgen studies showed typical skeletal and mastoid findings plus the suture spreading with moderate communicating hydrocephalus found after the August, 1963 admission (Fig. 3, *A-C*).

Meningeal biopsy was normal.

Therapy included 6 mercaptopurine, amethopterin, tetracycline, roentgen therapy, cytoxan, and steroids.

CASE III. D.H. is a white male of 4½ years. Seborrhea, exophthalmus, and roentgen skull changes were recorded elsewhere in May, 1962, and a biopsy in 1962 showed typical histiocytosis-X. In reviewing the early history, all systems were found to be involved, including the gastrointestinal tract. He did not have diabetes insipidus.

The laboratory findings were normal. Serum osmolalities varied from 288 to 300 milliosmoles and that of the urine was 780 milliosmoles.

The roentgenographic examination revealed, besides the classic bone changes, suture widening which was discovered in September, 1963 (Fig. 4), and evidence of communicating hydrocephalus (Fig. 5, *A* and *B*). The angiogram merely showed changes secondary to hydrocephalus, yet at the time of the ventriculography and biopsy no increased pressure was recorded.

The dural biopsy was positive for histiocytosis-X.

His therapeutic regimen included cortisone, velban, 6 mercatopurine, irradiation, and methotrexate intrathecally.

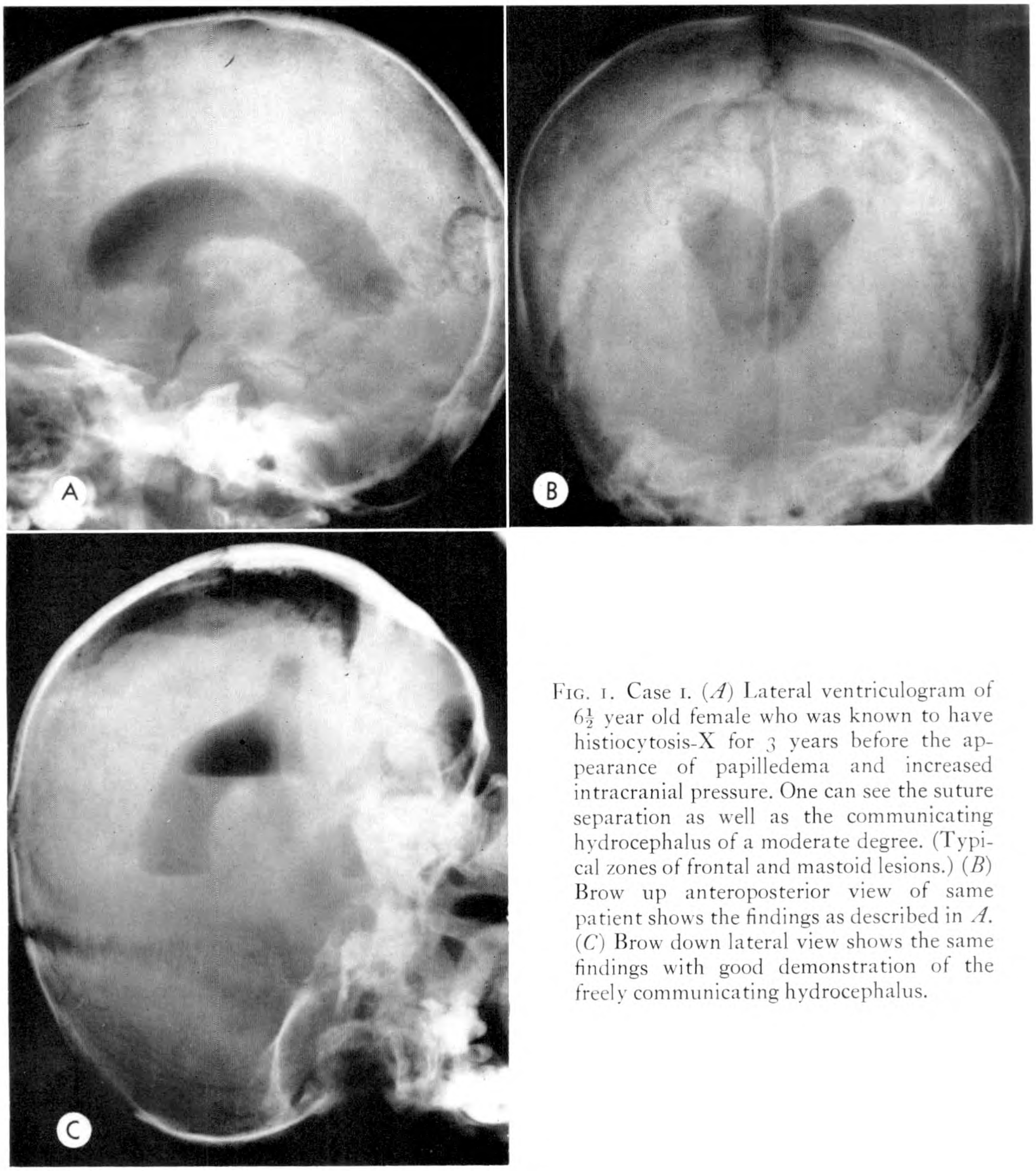

Fig. 1. Case i. (*A*) Lateral ventriculogram of $6\frac{1}{2}$ year old female who was known to have histiocytosis-X for 3 years before the appearance of papilledema and increased intracranial pressure. One can see the suture separation as well as the communicating hydrocephalus of a moderate degree. (Typical zones of frontal and mastoid lesions.) (*B*) Brow up anteroposterior view of same patient shows the findings as described in *A*. (*C*) Brow down lateral view shows the same findings with good demonstration of the freely communicating hydrocephalus.

Case iv. N. K. H. is a $3\frac{1}{2}$ year old female. In the fall of 1962 she had cervical lymphadenopathy assumed to be inflammatory and therefore she was subjected to a tonsillectomy in December, 1962. In January, 1963, petechiae, splenomegaly, otitis, and lymphadenopathy led to a biopsy and a diagnosis of histiocytosis-X.

She was first seen at the University of Minnesota Hospitals in May, 1963, with the typical multiple system involvement. On her third admission, the cervical lymphadenopathy had broken down and drained. She had an *E. coli* urinary tract infection. On her subsequent out patient visit, left proptosis was found. On her fourth admission in December, 1964, in addition to her chronic findings, diabetes insipidus was confirmed. Chemotherapeutically induced oral ulcerations were noted. There was left proptosis and chemosis. In spite of the orbital proptosis, no papilledema was present at that time.

The laboratory studies were basically normal insofar as the routine procedures were concerned. The proteins were somewhat depressed. The lumbar tap pressure was 208 mm. water. *E. coli* was cultured from the urine. The urine concentration was abnormal and the urine osmolalities increased from 136 milliosmoles to 490 milliosmoles after pitressin. The serum value after pitressin was 295 milliosmoles. The urine specific gravity was less than 1.005 and increased to 1.014 after pitressin.

The roentgenographic examination revealed considerable skull and orbital destruction. An interesting finding in December, 1963 was that of moderate suture separation. Not until December, 1964, was this studied clinically. By that time the suture separation had decreased appreciably, to the point of being only minimal. This probably can be correlated with the absence of recorded papilledema in December, 1964. Her ventriculogram showed minimal communicating hydrocephalus. (Because of their similarity to the findings of Cases I-III, although less marked, the roentgenographic reproductions are not presented.)

The therapeutic measures included irradiation, mycostatin, amethopterin, steroids, pitressin, N. I. H. eosinophilic granuloma plasma, tetracycline, and intrathecal methotrexate.

TOTAL CASE MATERIAL

Forty-one cases of histiocytosis-X, adult and pediatric, were collected from the files of The University of Minnesota Hospitals, from 1932 to the time of writing. This number includes the 4 cases detailed above. The study to evaluate the incidence of increased intracranial pressure first and central nervous system involvement secondly is summarized in Table I. As manifested by suture spreading, 6 cases had definite increased pressure; 2 more were equivocal. In addition, postmortem studies were positive for central nervous system changes of various degrees and localization without roentgen evidence of increased pressure in 8.

DISCUSSION

Some 41 years have passed since Letterer[8] and some 32 years since Siwe[9] first described this entity. Throughout the years volumes of material have been published; these will not be reviewed again. Two survey papers and the relatively recent paper dealing with the gastrointestinal

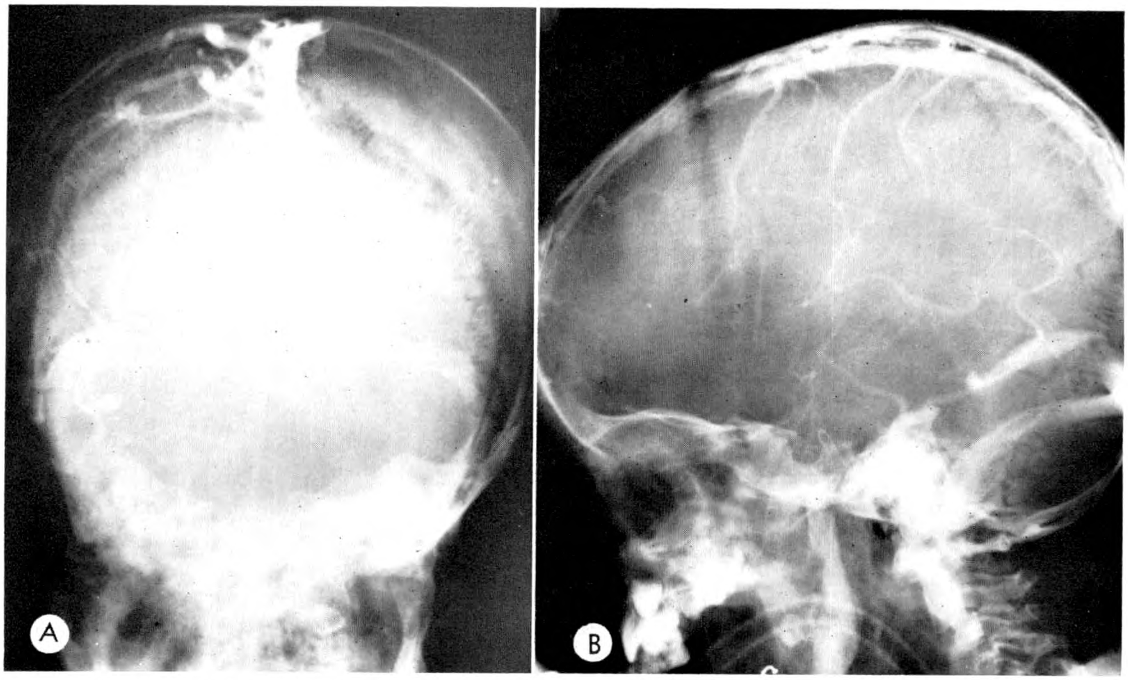

FIG. 2. Case I. (*A*) Anteroposterior dural sinus view of cerebral angiogram shows no evidence of invasion or obstruction of sinuses. (*B*) Lateral view of same angiographic phase shows normal sinus opacification.

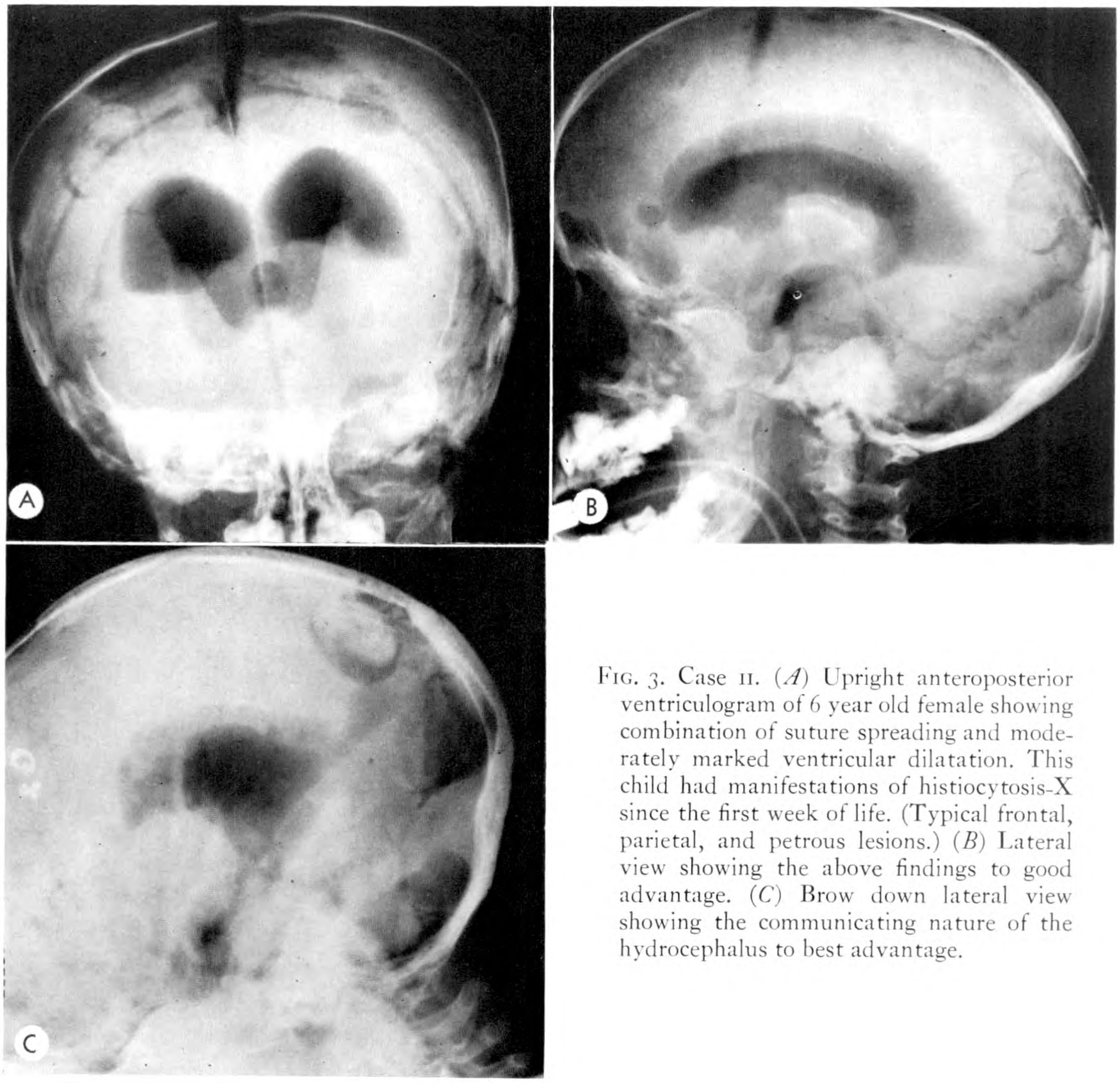

FIG. 3. Case II. (*A*) Upright anteroposterior ventriculogram of 6 year old female showing combination of suture spreading and moderately marked ventricular dilatation. This child had manifestations of histiocytosis-X since the first week of life. (Typical frontal, parietal, and petrous lesions.) (*B*) Lateral view showing the above findings to good advantage. (*C*) Brow down lateral view showing the communicating nature of the hydrocephalus to best advantage.

manifestations of the disease are cited for reference and complete bibliographies of conventional phases of histiocytosis-X.[1,3,4] There is little if any mention of increased intracranial pressure and hydrocephalus in spite of many cases of diabetes insipidus in children with histiocytosis-X. A recent paper negates the place of histiocytosis-X in neurologic problems.[5] Avioli *et al.*[2] reported a case of a patient with Hand-Schüller-Christian disease with hypothalamic involvement and hydrocephalus. In unrelated entities, hypothalamic disease associated with absence of thirst and hydrocephalus,[7] as well as hypothalamic involvement associated with hyperosmolarity and hydrocephalus,[10] may be suggestive of related mechanisms. Inflammatory mastoiditis with secondary invasion and obstruction of the dural sinuses has been reported,[6] and this phenomenon can also be considered as having a physically comparable role in histiocytosis-X even though etiologically unrelated. This was observed in 2 postmortem examinations in this series.

One can probably postulate from the above mentioned findings that increased intracranial pressure in chronic cases of histiocytosis-X should be kept in mind as a possible complication. A single etiology is obviously unlikely in view of the multiple

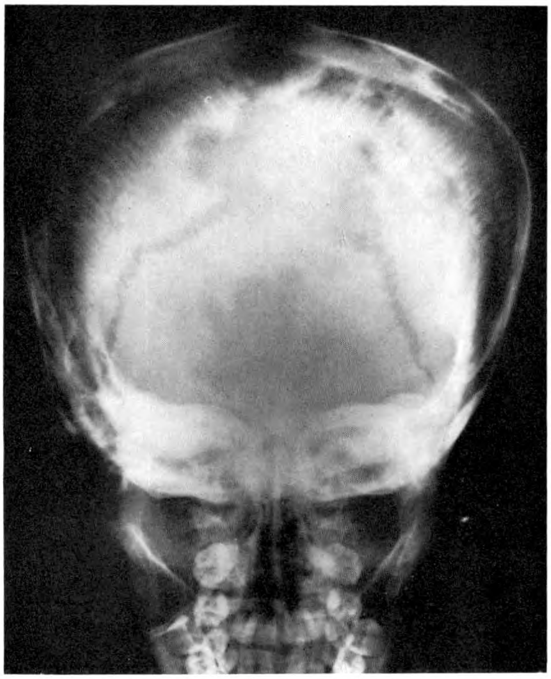

Fig. 4. Case III. A known case of histiocytosis-X in a $4\frac{1}{2}$ year old male who has had proved lesion for $1\frac{1}{2}$ years prior to evidence of increased intracranial pressure. The suture separation is marked. (Extensive typical bone lesions throughout skull.)

sites of involvement and the diverse factors implicated.

In Cases II and IV which have diabetes insipidus, the problem may be correlated with some degree of hypothalamic replacement.[2,7,10] One of our cases was found to have at postmortem examination such involvement.

Our current cases did not exhibit dural sinus invasion with obstruction roentgenographically; however, at least 1 of the postmortem cases showed superior sagittal sinus invasion and obstruction, and another showed petrous ridge replacement with sigmoid sinus encroachment. The over-all range of the biopsy and postmortem examination included the simple identification of cerebral histiocytosis-X cells to demonstration of thickened dura, meningeal, and underlying cortical involvement.

Although only 4 cases described herein had successful air studies and 2 had angiography, roentgen evidence of increased pressure was present in 6 and suspected in 2 more. An additional 10 cases had various degrees of central nervous system complications without premortem roentgen studies or roentgen evidence of increased pressure.

Obviously, one cannot incriminate one common denominator as the cause of the increased pressure. Instead, based on the multiplicity of histologic-anatomic localizations, one must postulate a variety of causes; *i.e.*, dural sinus invasion and obstruction; hypothalamic replacement with secondary electrolyte and fluid imbalance affecting cerebrospinal fluid production and

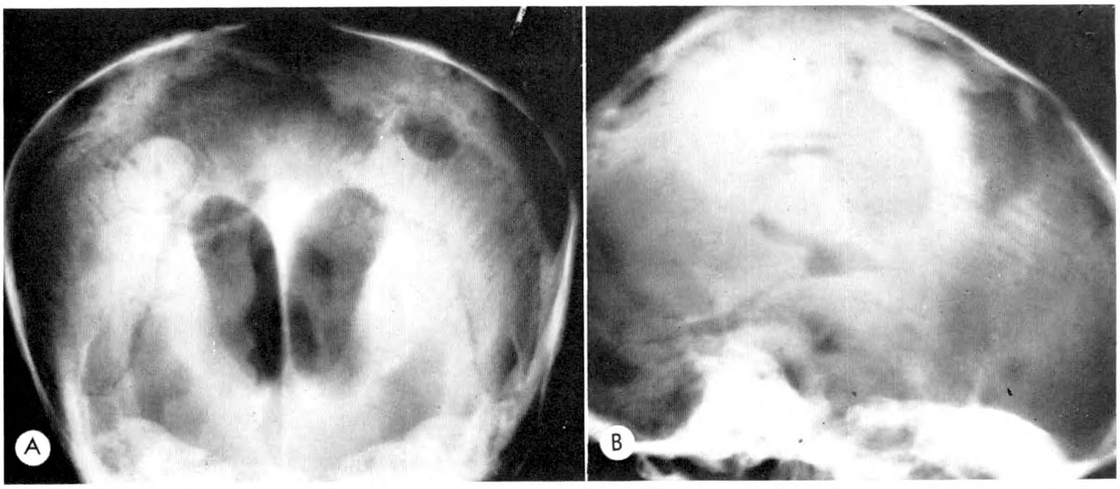

Fig. 5. Case III. (*A*) Anteroposterior ventriculogram showing moderate ventricular dilatation. (*B*) Lateral autotomogram showing excellent demonstration of the communicating nature of the hydrocephalus.

circulation as might be anticipated in severe diabetes insipidus cases; choroid plexus replacement; interference with cerebrospinal fluid absorption incident to dural or meningeal space obliteration, which conceivably could result in obstructive hydrocephalus depending on its location. The latter was not encountered in our group of cases. It is difficult to incriminate nonspecific edema even though one of the neuropathologic postmortem reports alluded to this.

Thus the place of roentgen examination in this problem is two-fold: (1) to suggest or confirm the presence of increased intracranial pressure; and (2) to attempt to pinpoint the specific type of involvement which is responsible for the increased pressure in the individual case, thereby possibly facilitating a more specific therapy.

SUMMARY

A "new" roentgen finding of increased intracranial pressure with communicating hydrocephalus is described in histiocytosis-X. Unlike the broad range of multiple system involvement in acute and subacute forms, the increased pressure findings appear to be limited to the chronic stages of the disease. We did not encounter a case of obstructive hydrocephalus but this can be postulated as a possibility.

One should not hesitate to obtain periodic skull studies in children with chronic histiocytosis-X in order to detect the insidious cases of increased pressure before eye signs, etc. are apparent. Such insidious course was present in Case III.

Apart from survey skull studies, air and angiographic examinations are recommended to determine if hydrocephalus is present and also if there might be a sign of dural sinus invasion.

The 41 cases of histiocytosis-X at The University of Minnesota Hospitals were reviewed. Six had definite roentgen evidences of increased intracranial pressure, 2 had suspicious evidence, and 10 had postmortem changes of the central nervous system.

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HODGKIN'S DISEASE IN CHILDREN*

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MOST parents when told that their child has Hodgkin's disease resort to medical textbooks for further information. Almost invariably they discover that the condition is considered incurable. It is now accepted, however, that the patient with Hodgkin's disease confined to one regional lymph area can be cured by radical radiation therapy.[1] The author has undertaken a review of the course of the disease in children and the results of treatment in 42 cases seen in the decade 1950–1959 inclusive at the Christie Hospital are here reported.

The sex ratio in the 42 cases of Hodgkin's disease was 28 males to 14 females or exactly 2 to 1 in favor of males. The youngest patient was 3 years of age and there was a relatively even distribution of cases from the age of 8 years upwards. In all of these cases the diagnosis was confirmed by histologic examination. The diagnosis of Hodgkin's paragranuloma was made in only 2 cases, one a male who is alive and well 6 years after treatment and the second a female who is alive and well 10 years after treatment. The sarcomatous type of Hodgkin's disease was diagnosed histologically in 1 case; this patient died within 3 weeks of being seen, with a rampantly progressive illness.

Tuberculosis is frequently the first diagnosis made in patients subsequently proven to have Hodgkin's disease and the association of Hodgkin's disease and tuberculosis is well known.[4] One case in the group had both Hodgkin's disease and tuberculosis of the cervical lymph nodes. The disease was generalized when the dual diagnosis was made and the patient survived only 6 months.

SITE AND STAGING

An attempt at clinical staging was made as a guide to treatment and prognosis and usually it was specified whether the disease was localized or generalized. The term localized disease was applied to those cases where there was involvement of only one lymph node region or of two lymph node regions in continuity, *i.e.*, right side of neck and right axilla. The term generalized disease was applied to all other cases whether or not the patient had systemic symptoms, *i.e.*, pruritus, pyrexia, weight loss, anemia, etc. In the 42 cases, 14, or 33 per cent, were classified as having generalized disease when first seen. Of 28 with localized disease, one regional lymph node area was involved in 24 instances and 2 lymph node areas in continuity in 4 cases. The sites of the disease in the localized cases were as follows: right side of neck (12 cases); left side of neck (9 cases); right and left side of neck (2 cases); right neck and mediastinum (1 case); left neck and mediastinum (1 case); left axilla (1 case); left groin (1 case); and abdomen (1 case).

SIGNS AND SYMPTOMS

The cervical lymph nodes were palpable in 25 out of the 28 cases with localized disease. Of patients who were found to have generalized disease when first examined, 7 had gone to their family doctor complaining of a lump in the neck. As a presenting sign, therefore, enlarged cervical lymph nodes were noted in 32, or almost 80 per cent of the 42 cases.

The predominating symptom was a palpable lymph node in 27 of the 28 cases with localized disease. Abdominal pain was the symptom in the other case. When the disease was generalized, the symptoms were more diverse. These included: a mass in the neck (7 cases); a mass in the axilla (1 case); malaise, itching, pyrexia (3 cases); generalized enlarged lymph nodes (1 case); multi-

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* From Christie Hospital and Holt Radium Institute, Manchester, England.

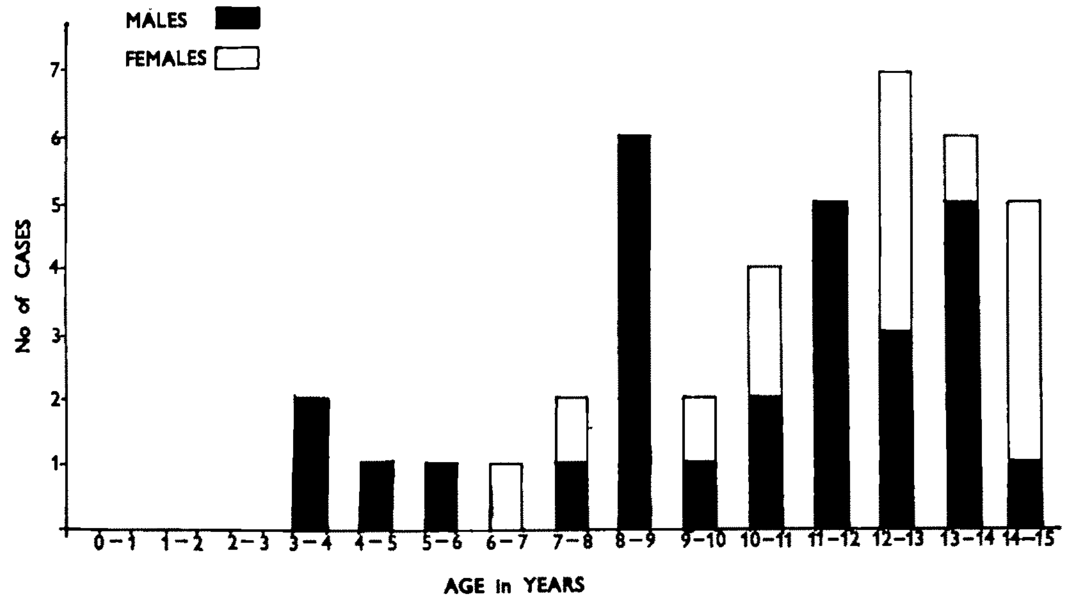

Fig. 1. Age and sex distribution of Hodgkin's disease in children.

ple skin lesions (1 case); and abdominal pain (1 case).

The duration of the presence of the enlarged lymph nodes in the cases with generalized disease varied from 3 weeks to 4 years. In the localized group the time intervals were: under 1 month (12 cases); 1 to 3 months (3 cases); 3 to 6 months (6 cases); and over 6 months (2 cases). In 2 cases, the duration of symptoms was not specified.

BLOOD

There was a mild degree of anemia in these patients. Hemoglobin estimations varied from 50 per cent to 106 per cent with a mean of 83 per cent. The white blood cell count varied from 4,300 to 32,000 per cubic mm. with a mean figure of 8,800 per cubic mm. The classic polymorphonuclear leukocytosis[5] was frequently seen with a mean figure of 68 per cent of polymorphonuclears in the blood films.

ROENTGEN FINDINGS

In 24 per cent of the cases in this series, enlarged hilar or mediastinal lymph nodes were demonstrated when the patient was first seen. Of 32 cases with negative findings on initial chest roentgenograms, 19 subsequently became positive. This occurred at time intervals varying from 3 weeks to 6 years, 8 months, with a mean time interval of 3½ years. The disease usually manifests itself in the chest by enlargement of lymph nodes, but in 3 cases there was pulmonary parenchymatous infiltration with Hodgkin's granulation tissue. Bone involvement was only seen in 1 case where there was a solitary lesion of the 4th lumbar vertebra.

CLINICAL COURSE

The clinical course of Hodgkin's disease can be divided into 3 stages: (a) localized disease in one or two lymph node areas; (b) disease which has become generalized with enlarged lymph node masses in different areas, superficial or deep, and often associated with enlargement of the spleen or liver; and (c) late generalized disease with marked weight loss, pyrexia, weakness, pruritus, anemia and often a hemolytic blood picture which does not respond to transfusions or steroid therapy.

These 3 stages are usually quite distinct though progression occurs unless the disease is cured in the early stages. The importance of recognizing each stage is that it gives the clue to management. In the early localized disease, cure is possible and should be attempted. When the disease is generalized but without systemic upset, radiation treatment alone can dispose of unsightly lymph node masses and keep the patient free of symptoms and leading a relatively normal life. When systemic symptoms occur, chemotherapy is best used and HN_2 is perhaps the most potent antipyretic in the management of Hodgkin's disease.

The stages of the disease in children appear to be the same as in adults, but the clinical course progresses more slowly. In the reported group of children, the male cases which proved fatal survived an average of 4 years, 10 months, while the comparable figure in the female cases was 3 years, 1 month. In all, 8 cases survived for more than 5 years.

TREATMENT

The treatment policies in the management of this disease vary widely. Opinions differ on the relative values of radiation therapy and chemotherapy in the early stages of the disease. We believe that localized disease should be treated on a local basis, *i.e.*, by radiation therapy and that chemotherapy, which of necessity must affect all the reticuloendothelial tissue in the body, should be reserved for the cases showing generalized disease. Hodgkin's disease is probably unifocal in origin and curable when confined to one lymph node area. The various types of treatment given to the 42 cases were: radical surgical excision (1 case); chemotherapy only (4 cases); radical radiation therapy (19 cases); radical radiation therapy with chemotherapy (2 cases); and palliative radiation treatment (23 cases).

SURGERY

The patient who had a radical excision of the lymph nodes in the left side of the neck is alive and well 11 years later.

RADIATION THERAPY

Thirty-six patients received radiation treatment and in 21 cases the treatment was aimed at raising a localized volume of tissue to maximal dose in the hope of curing the disease. The technique employed in most cases was that of the Manchester trunk bridge technique as described by Easson *et al.*[2] When the disease becomes generalized and distant lymph nodes show enlargement, palliative radiation treatment is given by an infinite variety of field sizes adapted to the anatomy of the region being treated. The aim of treatment here is to resolve local lymph node masses with the minimum application of roentgen rays so that the patient may be kept as comfortable as possible.

CHEMOTHERAPY

Since the discovery of the nitrogen mustards, Hodgkin's disease has been treated with a number of compounds with varying degrees of success. The preparations which were used in this series were:

(a) Triethylenemelamine (T.E.M.). This was used in 12 cases. Nine showed no response and 3 had a short response which in no case lasted more than 4 months. An oral mustard preparation is attractive when treating children but the response here was poor.

(b) Steroids were used in 9 cases. It is difficult to determine their exact value because of the fact that they generally were given late in the course of the disease—on average only 3 months before death. There is no doubt that steroids improve the sense of wellbeing and the patient may become quite euphoric. They also help to improve the terminal hemolytic anemia, but in most cases the disease usually continues to advance even when high dosage steroid therapy is administered.

(c) Nitrogen mustard. HN_2 was given in 8 cases and proved to be the most reliable chemotherapeutic agent, although again it appears that often it was administered too late for any real hope of response. Four patients showed an excellent response with remissions extending up to 1 year. Three cases died within 1 month of receiving HN_2 but even in these cases there was a temporary, though transient, response. Only 1 case showed no response to HN_2 therapy. The drug was administered on a weight basis, *i.e.*, .4 mg./kg. body weight, and no untoward effects were seen other than the usual leukopenia, etc.

(d) A miscellaneous group of chemotherapeutic agents was used in individual cases. Thiotepa and V. L. B. produced limited short response. No response was obtained from trillekamine, endoxana, chlorambucil and "9859" experimental.

RESULTS

Of the total group of 42 cases, 30 died of their disease and 12 are still alive. Of those who died, 22 were males and 8 were females. Of the males, 7 survived less than 1 year, 6 survived more than 1 year but less than 3 years, 3 survived more than 3 years but less than 5 years, and 6 survived more than 5 years. Of the 6 males still living, 2 are alive over 10 years and 4 are alive more than 5 years but less than 10 years.

Of the 8 females who died, 3 survived less than 1 year, 2 survived more than 1 year but less than 3 years, 1 survived more than 3 years but less than 5 years and 2 survived more than 5 years. Of the 6 who are still alive, 2 are alive over 10 years, and 4 are alive more than 5 but less than 10 years.

DISCUSSION

The place of radiation treatment in the management of the lymphoreticular disease is fully established. Early localized disease is curable and almost every other case obtained palliation of a high order with minimal discomfort. The addition of chemotherapy to radiation therapy has little to recommend it unless each is indicated in its own right. Paterson[3] has suggested that whatever agent is used first the benefit obtained is much greater than with any subsequent therapeutic agent.

A more controversial aspect of the use of radiation therapy is the question of dose. When treating localized malignant disease, the tendency is to obtain maximum effect, yet 3 of the survivors in the reported series who were treated with dosages which were palliative in intent are alive and well at 5, 10 and 11 years, respectively, without any evidence of disease. On the other hand, the lower doses given in palliative procedures in other cases have failed to produce complete resolution of lymph nodes and in some cases frank recurrence in previously treated areas had occurred. It may well be that Hodgkin's disease shows a spectrum of sensitivity to radiation and this may be unrelated to the histologic features of the paragranuloma.

SUMMARY

Forty-two cases of Hodgkin's disease in children under the age of 15 years are discussed. The disease appears to progress more slowly in children than in adults—8 patients out of 30 who died survived 5 years after treatment. Twelve cases, or 29 per cent, are alive and well without recurrence of disease 5 years after treatment. In children, the prognosis appears to be better in females than in males.

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I wish to acknowledge the work of the pediatricians and radiotherapists of the Manchester Region who treated these cases.

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ROENTGEN THERAPY FOR VISCERAL JUVENILE XANTHOGRANULOMA, INCLUDING A CASE WITH INVOLVEMENT OF THE HEART*

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JUVENILE xanthogranuloma, or nevoxantho-endothelioma, is primarily a self-limiting skin disorder of infants and children. Occasionally, there is visceral involvement as well. When this occurs, significant morbidity can result before the disease runs its course. Distressing symptoms and deformity can be prevented by judicious radiation therapy. The total experience of the Radiation Therapy Section of the Walter Reed General Hospital is limited to 2 biopsy proven cases plus 1 case diagnosed on a clinical basis. Our most recent case presented with cardiac involvement, which is unprecedented in the literature. The unusual nature of the latter case and the relative paucity of reported experience in the use of radiation therapy for the treatment of this disorder prompts the following case reports.

REPORTS OF CASES

CASE I. (Included in a previous report.[9]) E.Q., an 8 month old white female, was admitted to Walter Reed General Hospital on July 13, 1957 following recurrent episodes of bleeding into the anterior chamber of the left eye. Physical abnormalities were confined to the eyes and the skin. The left iris was somewhat discolored and there was blood in the anterior chamber. There were several macular skin lesions located over the trunk.

A hemogram, urinalysis, serum cholesterol and roentgenograms of the chest and skull were normal. A skin biopsy was obtained with a pathologic diagnosis of juvenile xanthogranuloma. Glaucoma developed during hospitalization and a goniotomy was performed on August 9, 1957. The patient was referred for radiation therapy.

From August 21, 1957 to August 30, 1957 the left eye was treated through an anterior 5 cm. diameter field with 100 r per treatment to a total of 500 r to the surface of the eye in 5 treatments (200 kv. peak, 20 ma., 50 cm. target skin distance, half value layer 1.0 mm. Cu). On September 30, 1957 tonometry and funduscopic examination were normal. On February 17, 1958 the left iris had returned to normal color but there was an annular cataract forming a 4 mm. ring. Examination on May 11, 1958 revealed absorption of the lens of the left eye and a 13 diopter refractive error. A follow-up on August 8, 1964 revealed a darkened iris and elevated tension in the left eye. Vision had not improved. There has been no evidence of recurrence of the primary lesion.

CASE II. D.W., a 6 month old white male, was admitted to Walter Reed General Hospital on June 5, 1959 after two episodes of bleeding into the anterior chamber of the right eye. Examination revealed a steamy cornea, elevated intraocular tension, clotted blood in the anterior chamber, and a linear whitish-yellow opacity on the iris. The skin was free of lesions. The diagnosis of nevoxantho-endothelioma was made on clinical grounds and the patient was referred for radiation therapy.

From June 15, 1959 to June 29, 1959 the right eye was treated through an anterior 3.5 cm. diameter field with one treatment of 100 r and two treatments of 75 r for a total dose of 250 r to the surface of the eye (200 kv. peak, 20 ma., 43.5 cm. target skin distance, half value layer 1.02 mm. Cu).

On June 26, 1959 a fresh hemorrhage occurred and on July 2, 1959 the anterior chamber was irrigated and a biopsy was taken of the iris. The pathologic diagnosis was that of recent and organizing hemorrhages in the iris and the presence of giant cells of the foreign body type. A diagnosis of nevoxantho-endothelioma could not be established with the specimen. The patient was discharged on July 10, 1959 with no evidence of recurrent hemorrhage. His eye remained normal, except for postiridectomy changes, until 1962 when a cataract developed which enlarged slightly over the next 2 years. On September 24, 1964 it had stabilized. The eye was somewhat sensitive to bright light, but the child was not handicapped in any way in his activities.

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CASE III. J.C., a 3 month old white male, was noted to have lesions of the skin on the anterior chest and left forearm at birth. These had a raised firm yellowish-red appearance. During the last week of May, 1964 he had a severe cyanotic episode which recurred twice within a week. A chest roentgenogram (Fig. 1) showed marked enlargement of the cardiac silhouette and atelectasis of the left lower lobe. A thoracotomy was performed on June 1, 1964 which revealed a pericardial effusion of 120 cc. of bloody fluid. The major portion of the left lung was compressed, but re-expanded immediately with decompression (Fig. 2). There was a 2.5×3.5×2.5 cm. cauliflower shaped tumor located on the epicardium of the left ventricle between the anterior descending and circumflex coronary arteries. A smaller lesion was present on the left atrial appendage. Both of these lesions, as well as that of the left forearm, were biopsied. The pathologic diagnosis of all three was nevoxantho-endothelioma.

Postoperatively, the patient did well and was transferred to Walter Reed General Hospital on June 11, 1964. The two skin lesions (Fig. 3, *A* and *B*) at that time were about 2.5 cm. in diameter, had a yellowish-brown color and were firm to palpation. Blood cell counts, urinalysis, blood carotene level, total lipids, and serum cholesterol were within normal limits. The electrocardiogram suggested biventricular hypertrophy and showed T-wave changes consistent with postoperative pericarditis.

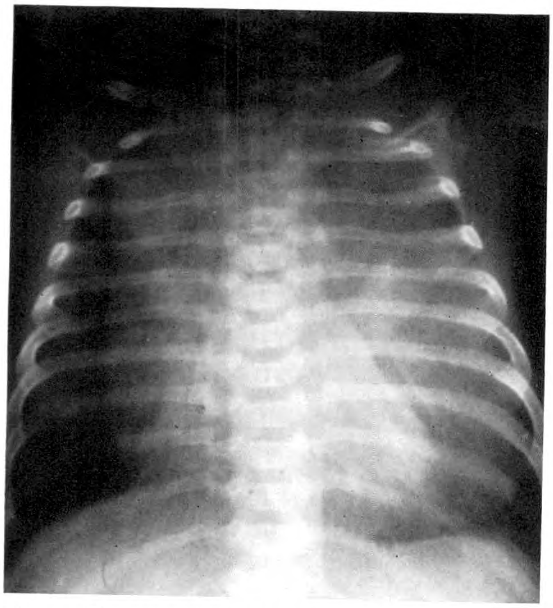

FIG. 1. Case III. Initial chest roentgenogram showing marked enlargement of the cardiac silhouette and atelectasis of the left lower lobe.

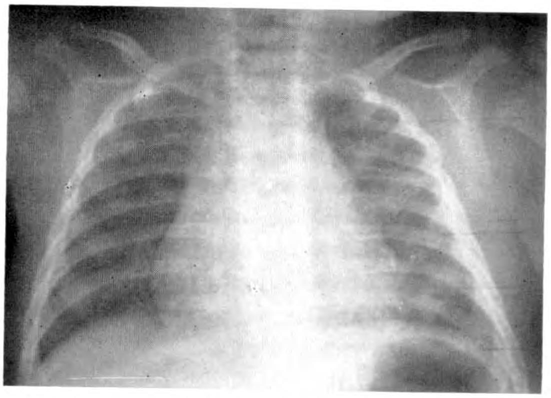

FIG. 2. Case III. Postoperative chest roentgenogram showing normal cardiac silhouette.

Because of the episode of hemopericardium from the cardiac lesions, it was decided to give a prophylactic course of radiation therapy. From October 14, 1964 to October 19, 1964 three treatments of 200 r tumor dose to the heart were given through an 8×7 cm. anterior chest field for a total tumor dose of 600 r (2 mv.

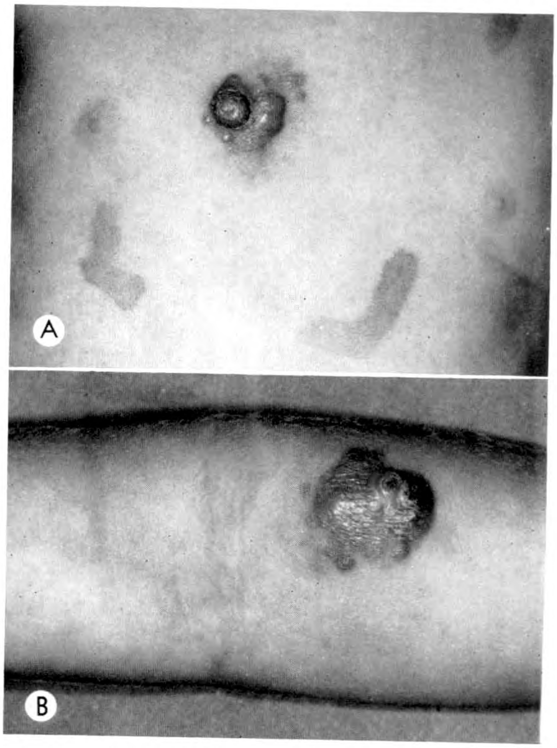

FIG. 3. Case III. Close-up studies of the anterior chest wall tumor (*A*) and left arm tumor (*B*).

peak, 1.5 ma., 100 cm. target skin distance, half value layer 7.0 mm. Pb). The skin lesions were not treated because they are known to regress spontaneously. The patient remained well, and on January 7, 1965 was showing normal growth and development. The skin lesions were unchanged in size, but had changed color to a golden yellow.

DISCUSSION

Nevoxantho-endothelioma was first described and named by McDonaugh,[10] although he was able to find a previous case report of a skin lesion which was probably this same entity. The disease is characterized by the appearance at birth, or soon thereafter, of multiple skin tumors over various parts of the body. There is a tendency to spontaneous involution within 6 months to 3 years. The skin eruptions appear as reddish-brown, orange, or yellow macules, papules, and nodules, varying in size from 1 mm. to several centimeters. Occasionally, there is a solitary lesion. Microscopically, these consist of histiocytes and varying numbers of foam cells within the dermis and subcutaneous tissues. Multinucleated giant cells are usually present and fat stains reveal the presence of intracellular lipid.[4,18]

There is apparently a relationship between this disorder and other xanthomas, but this lesion is differentiated on the basis of the presence of normal serum lipids. The etiology is unknown. This is considered by Crocker[3] to be the most benign type of xanthoma. Nomland[13] was able to find 42 cases in his search of Society Transactions Section of Archives of Dermatology and Syphilology. Of these, two-thirds had involuted by the age of 1 year. Stout[17] groups all xanthomas together and states that they are serious only because of their size and relationship to surrounding structures, with no mention made of invasion or destruction of normal tissues.

Over the years, there has been some disagreement as to the exact nature of this lesion, whether it is truly an endothelioma or a xanthoma.[7,15] A review of 53 cases led Helwig and Hackney[6] to conclude that nevoxantho-endothelioma was a misleading term. They felt that a more appropriate name would be juvenile xanthogranuloma, since no true endothelial cells could be identified. The histologic appearance will not be reviewed here, for it has been previously documented and well described.[6,12,14,18]

Reports of visceral involvement indicate that morbidity can be significant. There have been a number of cases reported involving the eye. Most of these involve the iris, produce glaucoma and hyphema, and can lead to blindness.[1,5,8,9,14] One case was epibulbar with encroachment upon the cornea.[2] There has also been a report of extraocular involvement with considerable destruction of the bony orbit and extension onto the overlying dura.[16] Lung and testicular lesions have been found, with simultaneous clearing of the lung and healing of the skin lesions in one case.[6,7]

TREATMENT

The skin lesions regress spontaneously, most within 1 year, and require no treatment.[3,4,13,18]

Radiation therapy has been employed successfully for eye lesions. Cleasby[1] treated an iris lesion using 200 r per treatment for a total of 600 r in 6 days (100 kv. peak, 20 ma., 24 inches target skin distance, half value layer 4.8 mm. Al). There was complete regression. Hedges[5] used 50 r (air dose) per treatment, giving 400 r total in 10 days (100 kv. peak, 15 ma., 24.5 cm. target skin distance, half value layer 3.0 mm. Al). He reported that the lesions disappeared 3 days after completion of treatment, and the eye appeared normal 2 months after treatment. Maumenee and Longfellow[9] reported treatment of 2 patients, one of whom (E.Q.) is included with a long term follow-up in this article. The second patient received 600 r for an iris lesion (50 kv. peak, 20 ma., 1.8 cm. target skin distance, half value layer 0.28 mm. Al). Within 15 months the lesions were nearly gone and the eye was reported normal after 4 years. No mention was made in any of these reports of cataract formation. The epibulbar lesions were surgically removed but recurred in 8 months.[2]

The two ocular lesions reported here responded with 500 r and 250 r dose to the eye surface. It is interesting that both of these patients subsequently developed cataracts, the former 6 months and the latter 3 years after treatment. Data presented by Merriam and Focht[11] indicate that 200 r should not produce a cataract, and that doses in the range used for our patients would have approximately a 50 per cent chance of producing cataracts. Unfortunately, there have been no reports of successful treatment of this disease using doses less than 250 r.

It is evident from the accumulated experience of various authors, as well as from these current case reports, that low doses of irradiation can produce regression of this lesion. One reported case of surgical removal failed because of recurrence. Since visceral involvement can produce significant complications, it would seem advisable to treat with 400–500 r in approximately 7 days when this diagnosis is made. In light of the response of one of our patients to a dose of 250 r, even lower doses may suffice. Indeed, because of the risk of developing cataracts when treating ocular lesions, a lower dose would be desirable.

SUMMARY

Juvenile xanthogranuloma, or nevoxantho-endothelioma, is primarily a benign, self-limiting skin disease appearing in the neonatal period. However, visceral involvement may occur with significant complications. Two cases of ocular involvement and a case with cardiac involvement have been described. Favorable results were obtained by treatment with low doses of external irradiation.

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THE MANY FACETS OF LYMPHANGIOMA

By RICHARD D. KITTREDGE, M.D., *and* NATHANIEL FINBY, M.D.
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THE lymphatic capillaries form a complex system of branching tubes. Their walls formed chiefly by endothelial plates show considerable variation in diameter and thickness. The larger lymphatic vessels are composed of three coats corresponding to those of veins. The internal coat is a thin, transparent lining composed of elongated endothelial cells supported on a thin elastic membrane. The middle coat consists of smooth muscle and fine elastic fibers arranged in a circular manner. The external coat is connective tissue intermixed with smooth muscle fibers.[1]

Lymph is propelled by contractions of the skeletal muscles, backflow being prevented by valves.

TYPES OF LYMPHANGIOMA

A lymphangioma is a tumor composed of lymphatic vessels. It is a mass consisting of endothelial cells and supporting connective tissue, both of which participate in the neoplastic process. Round cells, islands of fat cells and smooth muscle are usually present. Lymphangiomas are slow growing and frequently congenital. They appear in the skin, deep areolar tissue, muscle, lips, eye, mediastinum, retroperitoneal region and bone. Three general types are described.

1. *Simple Lymphangioma.* Simple lymphangioma is a rare congenital tumor which appears soon after birth; it is small and circumscribed in appearance. Following trauma, it exudes a serous fluid in the skin. The histologic structure consists of a network of spaces formed by small and medium sized vessels. The lining endothelium may be flat or cuboidal.

The simple lymphangioma grows slowly or remains stationary; it may appear whereever lymphatic vessels exist; it is commonly found in the skin and mucous membrane.

2. *Cavernous Lymphangioma.* Cavernous lymphangioma occurs usually in the skin but also in the mucous membranes and intermuscular septa. The dilated lymph spaces are filled with coagulable lymph, at times mixed with blood. The contents may be solidified and even calcified.

Analysis of the fluid may reveal blood proteins, salts, lymphocytes, exfoliated endothelial cells, and cholesterol crystals. The septa may be thin and cellular or they may be thick due to proliferating connective tissue and the presence of round cells, lymph follicles and smooth muscle.

3. *Cystic Hygroma.* A cystic hygroma is a benign, multilocular cystic tumor, the cavities of which are lined by lymphatic endothelium. Hygromas have a potentiality of almost unlimited growth, which is believed to be due to the fact that these "lymphatic nests" retain their embryonic power of irregular growth.[6]

ETIOLOGY

The etiology of lymphangioma is unknown. It may arise from lymphatic tissue normally present in the area or may grow directly from mesodermal rests which produce imperfect lymphoid channels. Bueno[3] has observed that certain cells of the reticuloendothelial system may be altered during infection and that the lymphatic tissue may be markedly altered. He reported increased swelling of a lymphangiomatous mass in the forearm following the injection of diphtheria antitoxin. The general opinion is, however, that the progressive nature of the disease is truly neoplastic.[5] The bone lesions certainly follow the general course of benign bone tumor.

REPORT OF CASES

CASE 1. This 42 year old female presented with the chief complaint of recurrent cystic masses in the neck (Fig. 1). One year prior to admission, she had been treated with morrhuate injection for this condition. Following admission, the mass was removed surgically.

The specimen consisted of a multilobulated partially collapsed cystic mass, 9 cm. in greatest diameter. It was tan to pink with a smooth ragged surface. Incorporated on the surface of the specimen were several discrete pink soft lymph nodes up to 1.5 cm. in diameter. The multicystic linings were smooth, tan and shiny. Microscopic examination revealed a fibrocollagenous adipose stroma with a few foci of smooth muscle and cavernous anastomosing channels, forming cysts filled with protein fluid and lined by flattened endothelial cells (Fig. 2). Lymphoid tissue with follicle formation was present in the septa. The pathologic diagnosis was hygroma of the neck.

Case II. This 10 month old male baby presented with an apparently painless mass in the neck. The clinical diagnosis was cystic hygroma and the mass was surgically removed.

The specimen consisted of a cystic mass which measured $5\frac{1}{2} \times 7$ cm. Its outer surface revealed a fibroadipose capsule. The tumor appeared to be composed of numerous cysts which measured from 1 to 3 cm. in diameter (Fig. 3). Beneath the capsule, the tumor was bluish purple in color. The cysts were filled with a brownish fluid which partially clotted. Microscopic examination revealed a tumor of fibrous stroma which varied from loose to compact structure in various areas. The cysts were lined by a single layer of flattened cells. The pathologic diagnosis was cystic hygroma of the neck.

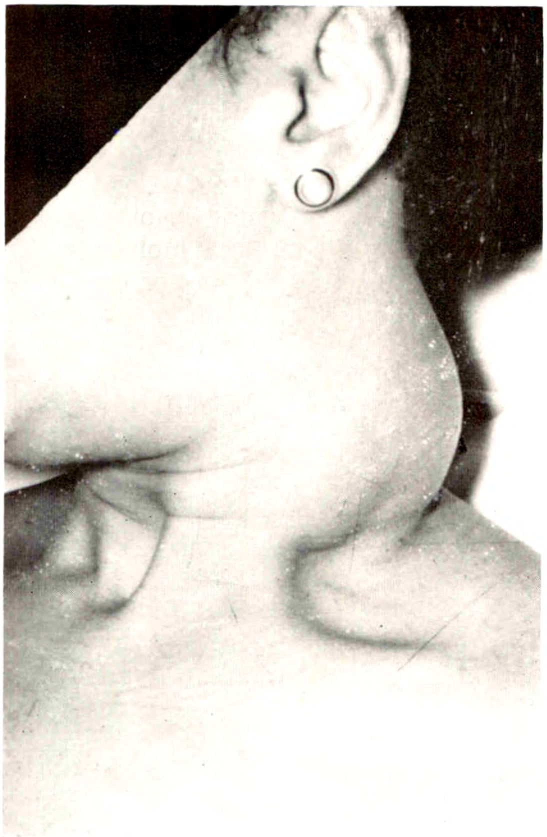


Fig. 1. Case I. Photograph showing recurrent cystic mass in the neck.

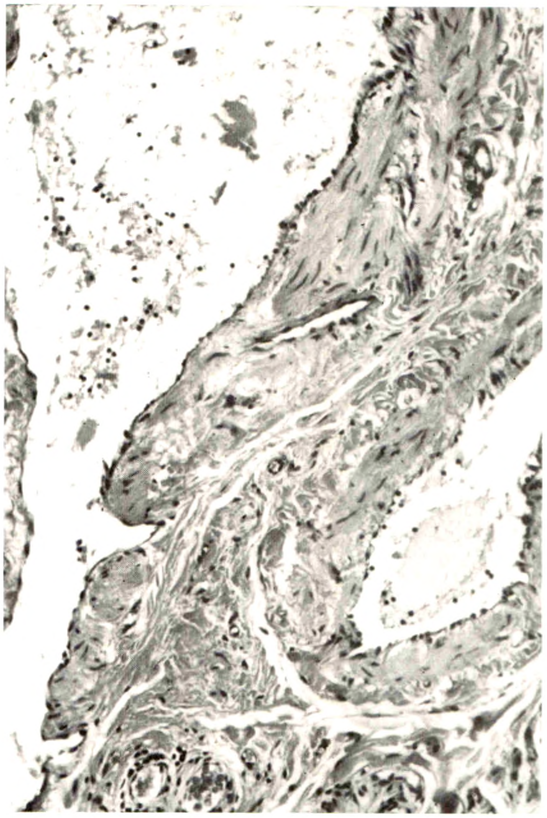


Fig. 2. Case I. The specimen consisted of a multilobulated partially collapsed cystic mass 9 cm. in greatest diameter. Microscopic examination revealed a fibrocollagenous adipose stroma with a few foci of smooth muscle. Cavernous channels forming cysts filled with protein fluid and lined by flattened endothelial cells were present. The pathologic diagnosis was hygroma of the neck.

Case III. This $4\frac{1}{2}$ year old female presented with the chief complaint of progressive crampy abdominal pain of 3 weeks' duration. A tumor had been felt in the abdomen and enlargement occurred during this 3 week period. The patient was operated upon shortly after admission.

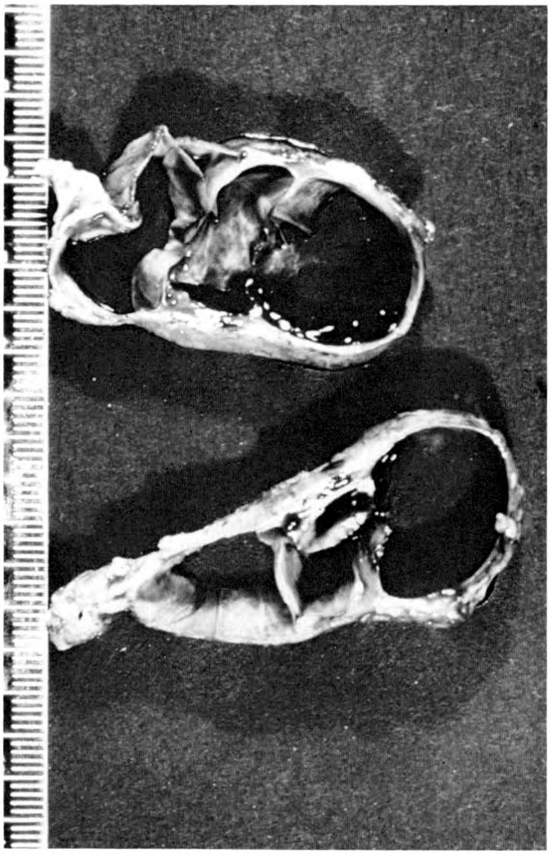


FIG. 3. Case II. The specimen consisted of a cystic mass which measured $5\frac{1}{2}\times 7$ cm. The tumor was composed of numerous cysts lined by a single layer of flattened cells. The pathologic diagnosis was cystic hygroma of the neck.

The specimen was a 47 cm. long segment of small intestine with mesentery (Fig. 4). The mesentery was yellowish white and the leaves of the mesentery were separated by a large multilobular cystic tumor mass which straddled a 9 cm. segment of bowel. Approximately 600 cm. of thick white fluid was present (Fig. 5). Microscopic examination revealed cavernous anastomosing channels lined by endothelium, and attachments to the muscle wall of the small intestine were present (Fig. 6). At the base of the mesentery, the channels appeared smaller. The diagnosis was cavernous chylangioma of the mesentery and jejunum.

CASE IV. A 3 week old female infant was hospitalized due to persistent vomiting. The patient was in a moribund condition and covered with regurgitated green bile. It was stated that the child was perfectly well until about 18 hours prior to admission, at which time she began to vomit and behave as if suffering from crampy abdominal pain. Delivery was said to have been completely normal. On the day of admission, the child passed two soft yellowish stools free of blood. Physical examination revealed a dehydrated child with shrunken fontanels. The abdomen was distended with a yellow moist crust on the navel. The rectum was empty.

A flat roentgenogram of the abdomen revealed marked gaseous distention of the stomach and pathologic distention of a few loops of small bowel (Fig. 7). There appeared to be associated fluid. The hemoglobin was 11.4 gm. per cent and the red blood cell count was 4.46 million. Five hours after admission, the patient died.

At autopsy, the peritoneal cavity contained approximately 300 cc. of opaque pale yellow milky fluid. The peritoneal surface appeared dull and was covered by a thick grayish white

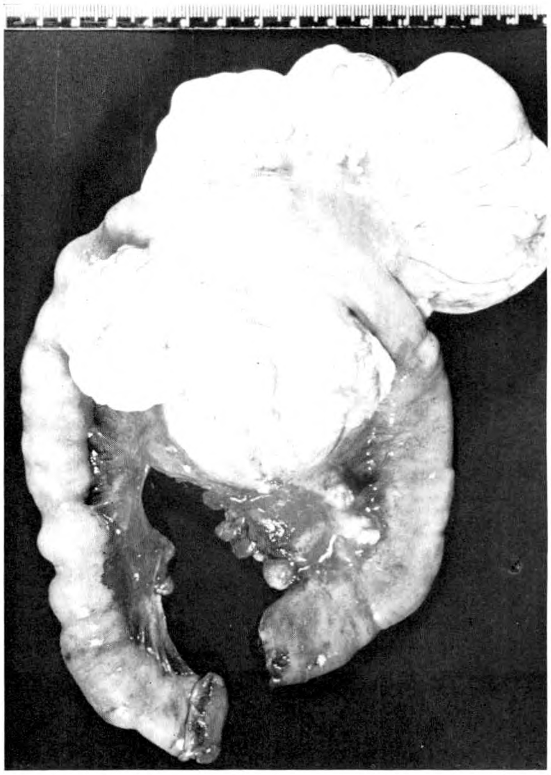


FIG. 4. Case III. The specimen was a 47 cm. long segment of small intestine with mesentery. The mesentery was yellowish white and the leaves of the mesentery were separated by a large multilobular cystic tumor mass which straddled a 9 cm. segment.

pasty-like material. Loops of small bowel were distended. The entire small bowel mesentery was 3 to 4 times thicker than normal macroscopically (Fig. 8 and 9). The small bowel was infarcted. Polymorphonuclear cells infiltrated all layers. Lymphatics in the submucosa and subserosal area were extremely dilated and filled with necrotic polymorphonuclear cells (Fig. 10). The mesentery of the bowel showed marked dilatation of lymphatics which ran into large cavernous channels filled with finely granular material. The endothelial lining was absent. A number of these channels was partially filled with degenerating polymorphonuclear cells. In the head of the pancreas, there were dilated channels in the interstitial tissue.

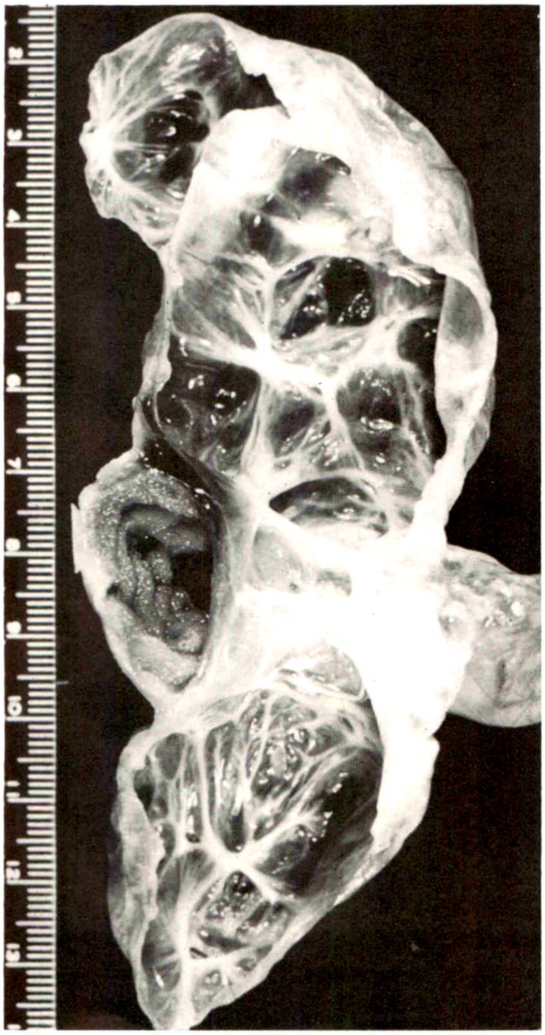


Fig. 5. Case III. Approximately 600 cc. of thick white fluid was present on sectioning the multilobular tumor.

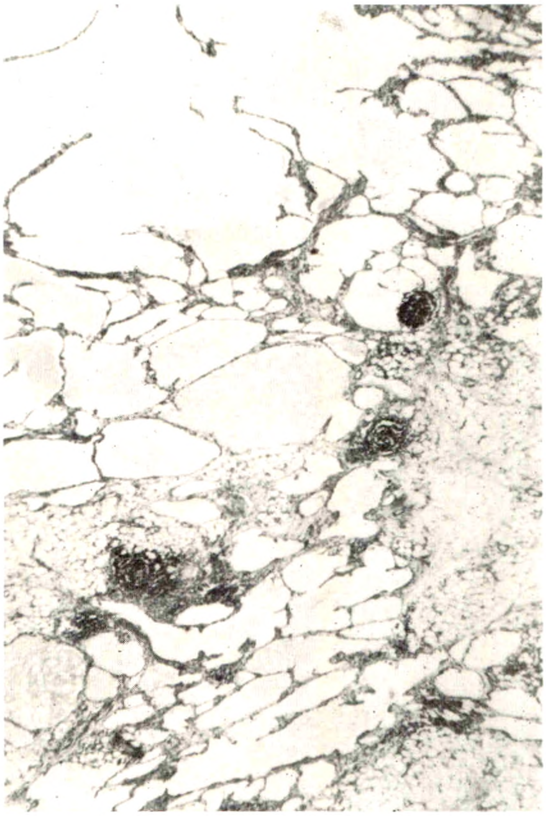


Fig. 6. Case III. Microscopic examination revealed cavernous anastomosing channels lined by endothelium. The pathologic diagnosis was cavernous chylangioma of the mesentery.

In summary, necropsy revealed a massive collection of chyle in the peritoneal cavity, a greatly thickened white mesentery with small bowel oozing chyle on section and a large segment of infarcted small bowel with mesenteric venous thrombosis. Microscopically, subserosa, submucosa and mesentery contained cavernous lymphatic channels filled with a protein material (chyle). It was felt that the findings represented primarily a chyle-lymphatic disease. This has been described as cholangioma cavernosum mesenterii.[12] Mesenteric venous thrombosis undoubtedly was due to mechanical obstruction from the pressure created by the cavernous lymphatic channels.

Case v. This 5 year old female presented with the chief complaint of recurrent attacks of abdominal pain, nausea and vomiting, and constipation every 4 to 6 months for a period of 3½ years. A roentgenogram of the abdomen showed several dilated loops of small bowel in

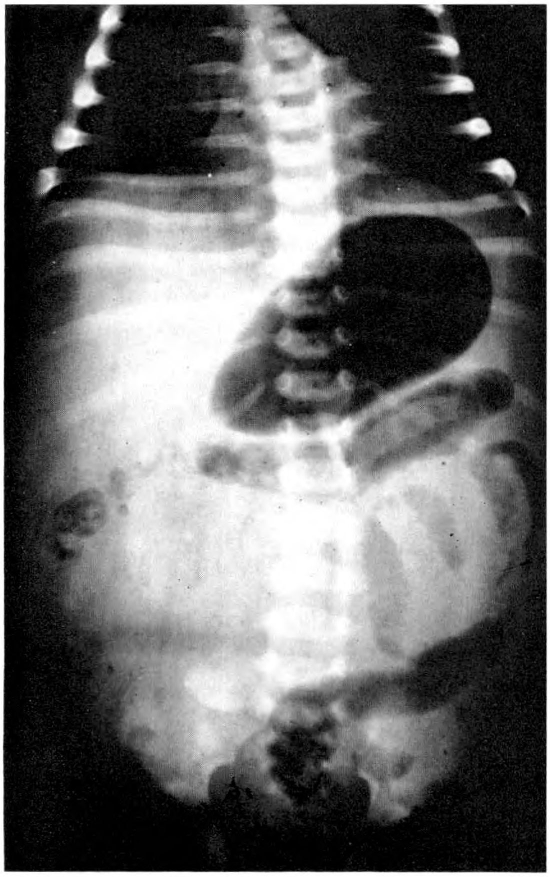


FIG. 7. Case IV. A roentgenogram of the abdomen showed distention of the stomach and pathologic distention of widely separated loops of small bowel, suggesting thickened walls and an edematous mesentery.

the upper abdomen. No gas was seen in the lower abdomen. The clinical impression was small bowel obstruction (Fig. 11). At operation, a segment of ileum was resected.

The specimen measured approximately 19 cm. in length and showed a cystically dilated sac in its middle part, approximately 14 cm. in greatest width (Fig. 12). This cystic structure extended into the mesentery. The intestinal serosa was pinkish tan, smooth and shiny. On opening the bowel, there was marked distention and stretching of the intestinal wall upon the cystic structure, which contained approximately 50–60 cc. of milky chylous fluid. The wall of the cyst was transparent, membranous and traversed by vessels and fibrous cords. The inner surface of the cyst was smooth and glistening. Microscopic examination of the cyst wall revealed fibrous connective tissue which, at the site of attachment to the ileum, showed numerous smooth muscle bundles originating from the thickened hypertrophied ileal muscular coat. In many areas, there was no apparent lining, while in other sites flattened endothelial-like cells were seen on the inner surface of the cyst. No intestinal epithelial lining was noted in the cyst. The pathologic impression was lymphatic cysts of the mesentery.

CASE VI. This 2½ year old boy presented with the chief complaint of edematous right upper extremity, periorbital edema, and a protuberant abdomen. The patient was the product of a full term delivery. At birth, lymphedema of the right upper extremity was noted. At the age of 1½ years, a lymphangioma of the right

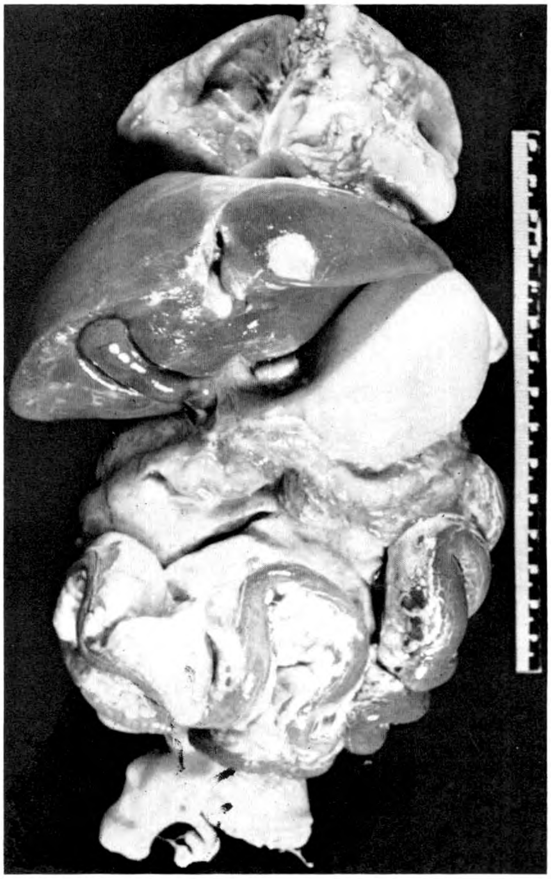
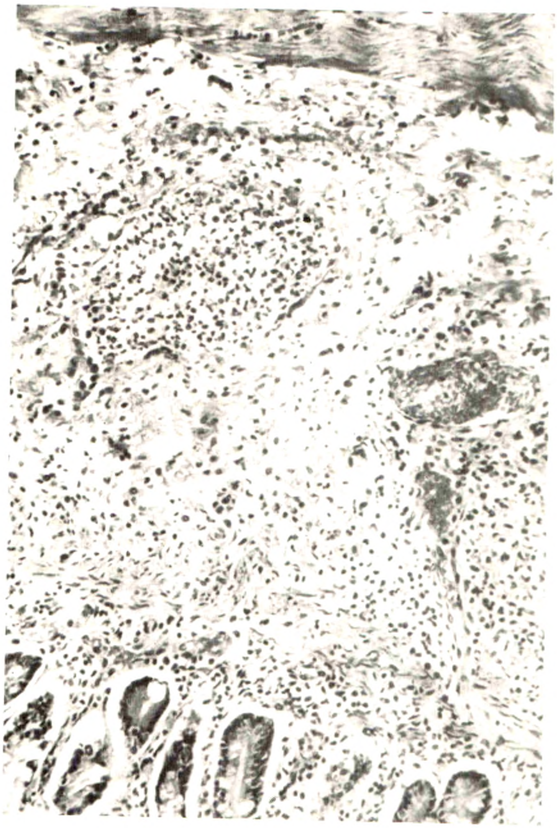


FIG. 8. Case IV. The thoracic and abdominal cavity contents were removed intact. The peritoneal surface appeared dull and covered by a thick grayish white pasty material. The small bowel was dilated and the mesentery was thickened. Three hundred cc. of free chyle was present in the abdomen.

Fig. 10. Case iv. Microscopic examination of subserosa, submucosa and mesentery showed cavernous lymphatic channels filled with chyle.



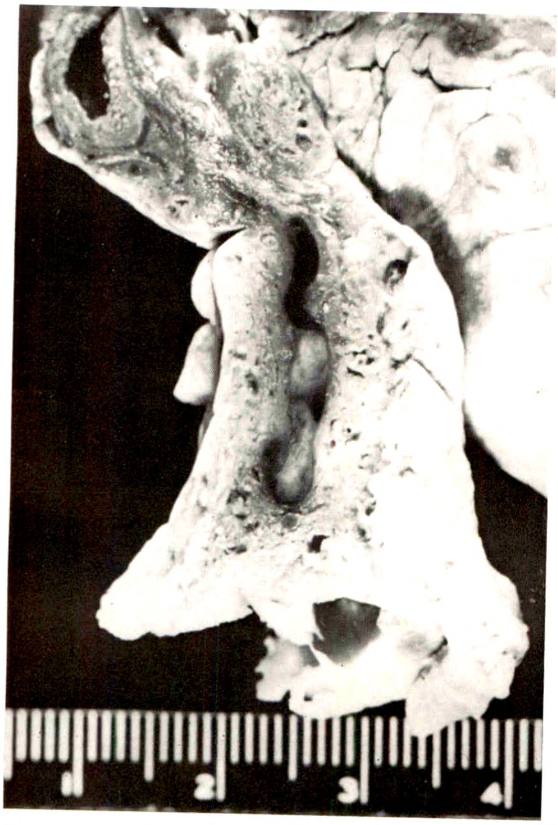
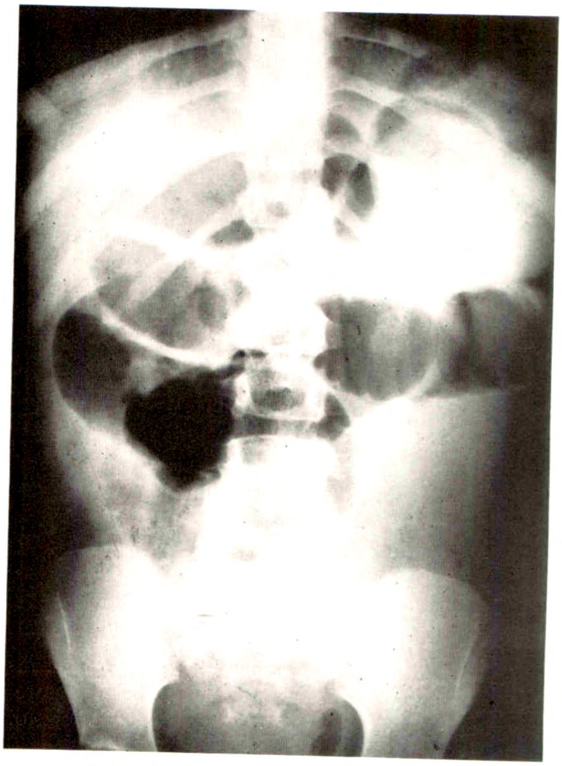


Fig. 9. Case iv. A section of bowel and mesentery showed marked thickening. A large segment of infarcted bowel was present which oozed chyle on sectioning.

Fig. 11. Case v. A roentgenogram of the abdomen showed several dilated loops of small bowel in the upper abdomen. No gas was seen in the lower abdomen. The clinical impression was small bowel obstruction.



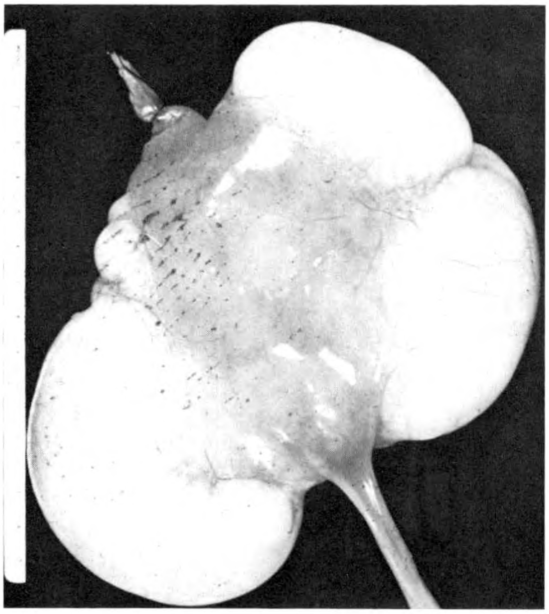


FIG. 12. Case v. A 19 cm. segment of ileum was resected. Associated with the bowel was a cystically dilated sac, 14 cm. in width. On sectioning the specimen, the bowel was found to be distended. The cystic structure contained 50–60 cc. of milky chylous fluid.

upper extremity was removed. Shortly after lymphangiectomy, he developed watery diarrhea up to 6 times per day, which persisted up to the time of his admission to our hospital. The diarrhea was partially controlled by placing the child on a celiac diet. During the last year he had had episodes of periorbital edema, ascites, peripheral edema, pallor, listlessness and diarrhea. The clinical impression at the time of admission was right upper extremity edema due to lymphatic drainage insufficiency following the removal of a lymphangioma, primary intestinal disease with exudative enteropathy and diffuse lymphatic disease.

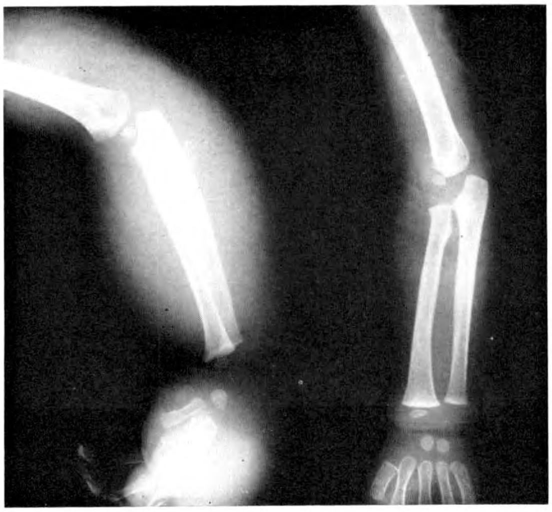


FIG. 13. Case VI. A roentgenogram of both forearms showed a large soft tissue mass in the right forearm with definite increase in the length and size of the bones.

A review of chemical examinations performed at the age of $1\frac{1}{2}$ years, at the time of the removal of the lymphangioma, showed a definite hypoalbuminemia without hypogammaglobulinemia.

Roentgenograms of both forearms showed a large soft tissue mass of the right forearm with definite increase in length and size of the bones (Fig. 13). The small bowel series showed a very abnormal mucosal appearance with a normal transit time. The mucosal folds were coarse and ragged (Fig. 14). There was loss of continuity of the barium column with definite clumping of the barium. The picture was consistent with exudative enteropathy. The right arm scar was re-biopsied. The microscopic examination showed atrophic squamous epithelium. The

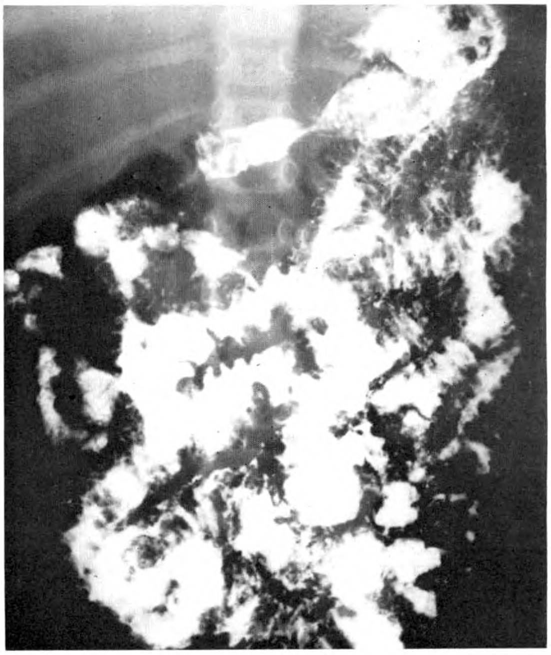


FIG. 14. Case VI. A gastrointestinal study showed a grossly abnormal small bowel pattern which was characterized by coarsening of the folds associated with minimal dilatation and increased secretions. The findings were consistent with exudative enteropathy.

dermis consisted of proliferated swollen collagenous fibers and foci of inflammatory cells beneath the skin. There were dilated lymphatics filled with granular precipitate surrounded by loose connective tissue and fat. The pathologic diagnosis was lymphangioma of the right arm. On April 25, 1963 the jejunum was biopsied. Broad villi were present. Several of these contained dilated lymphatic spaces (Fig. 15). There was no cellular infiltrate. The pathologic diagnosis was lymphangiectasis consistent with lymphangioma.

Case vii. This 15 year old male was referred to an endocrine clinic with the chief complaint of failure to grow. The patient showed objective evidence of slight decrease in growth and maturation.

A routine chest roentgenogram revealed a left superior mediastinal mass (Fig. 16).

The tumor was surgically removed and the patient has done well. The pathologic diagnosis was lymphangioma.

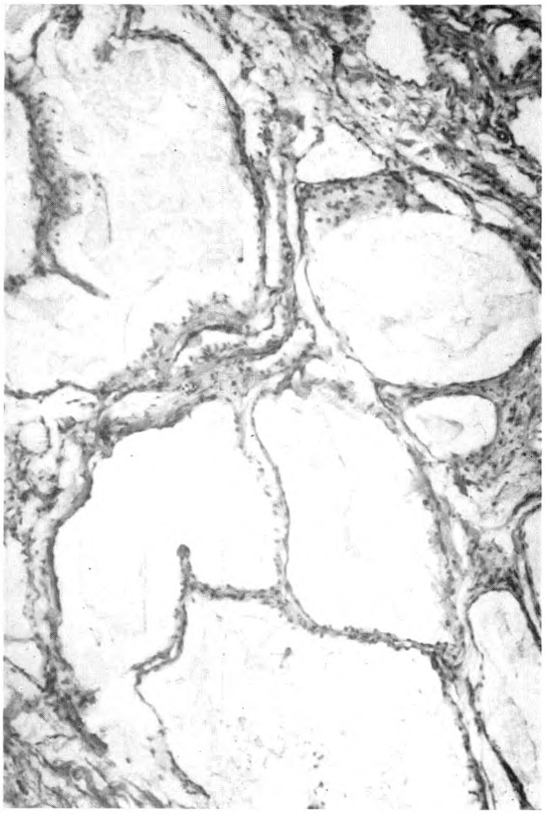


Fig. 15. Case vi. Microscopic examination revealed dilated lymphatic spaces.

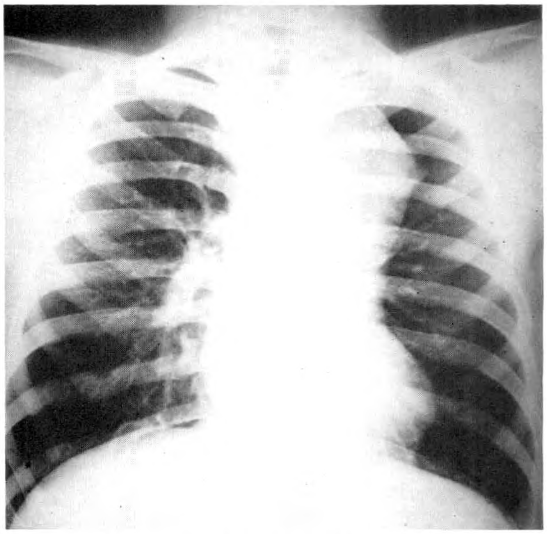


Fig. 16. Case vii. A chest roentgenogram showed a left superior mediastinal mass.

Case viii. This 15 year old boy entered the hospital with the chief complaint of painless lymphadenopathy in the left groin of 7 months' duration with some progression in size of the lymph nodes over this period. No fever had been present throughout this time. On physical examination, there was a soft, spongy subcutaneous mass in the inner aspect of the left thigh, measuring 21×15 cm. The impression was lymphangioma of the thigh.

Lymphangiography was performed by injection of contrast material into the dorsum of each foot via catheterized lymphatic vessels. A huge plexus of abnormal lymphatic channels and sinuses with gross disorganization of the normal lymphatic pattern was demonstrated throughout the thigh, inguinal area and pelvis (Fig. 17). The lymph nodes in the inguinal area were grossly abnormal (Fig. 18). The contrast material passed into a large mass along the inguinal area and deep pelvis to the presacral tissues. Venography performed on the right side revealed a normal right common iliac vein and a normal inferior vena cava up to the level of L1. At operation, a 26×14 cm. mass was removed from the left thigh.

Pathologically, the specimen appeared spongy. Chylous fluid exuded from all the cut surfaces. Microscopic sections showed diffuse growth of branching networks of dilated vascular channels lined by flat endothelium with varying amounts of smooth muscle bundles in their wall. The margins of the lesion were poorly defined. The upper margin of the resected mass

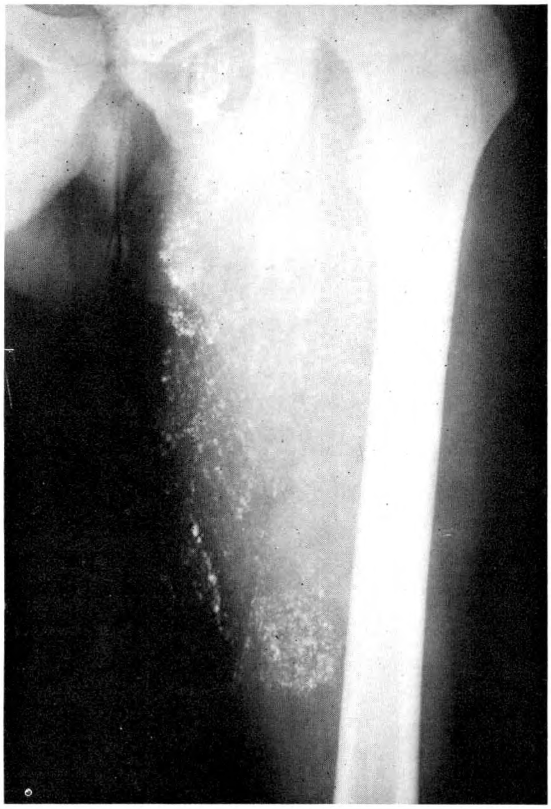


FIG. 17. Case VIII. A lymphangiogram showed a huge plexus of abnormal lymphatic channels and sinuses with gross disorganization of the normal lymphatic pattern.

contained tumor. There was no evidence of cytologic malignancy. The pathologic impression was lymphangioma of the soft tissues of the left thigh, extending into the inguinal region and pelvis.

Bone lesions in the pelvis, hip and shoulder were noted on roentgenograms (Fig. 19 and 20). Multiple lytic lesions of bone due to lymphangiomata have been reported. Histologically, the defects are produced by the pressure atrophy caused by dilated lymph channels.

DISCUSSION

Lymphangioma is a rare tumor which presents in various ways.[8,18] A soft tissue mass is by far the most common finding (Cases I, II, III, IV, V and VII). Bone involvement is seldom seen. In 1947 the first case of lymphangioma of bone was recorded.[2] The ilium in this 5 year old girl was almost completely destroyed. Radiation therapy had little effect. Other authors have reported multiple destructive lesions which progressed relentlessly despite surgery, curettage and radiation therapy.[4,10] In one of our patients (Case VIII), the bone lesions, which are probably lymphangiomas, have remained fairly stable for 3 years. The lesions are always lytic and well defined. There may be a peripheral zone of increased density.[9,15]

There is a group of patients who present with hypoproteinemia and edema as a result of loss of proteins into the gastrointestinal tract (Case VI) via a disorder in the lymphatic system of the small intestine.[7,11,13,14] The lymphatics of the mucosa and the mesentery of the small intestine are markedly dilated. This results in hypoalbuminemia, hypogammaglobulinemia, edema and effusions. Some patients who manifest this lymphangiectasia have also demonstrated chylous effusions and localized edema, indicating the generalized nature of the disease. Lymphangiography has demonstrated hypoplasia of lymphatics in

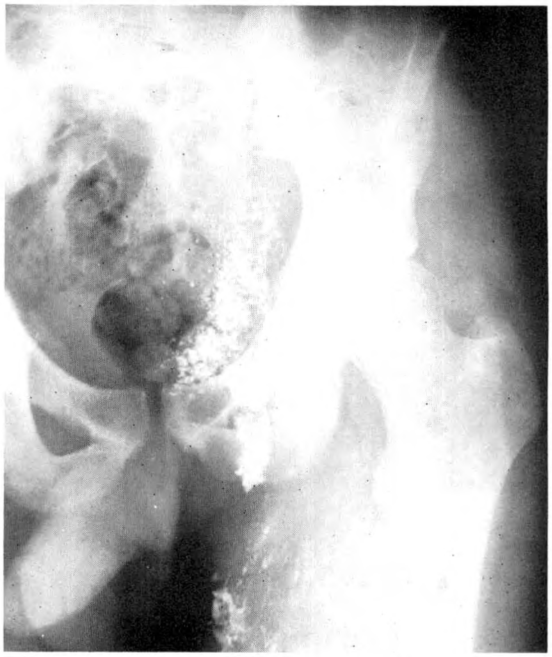


FIG. 18. Case VIII. A roentgenogram showed grossly abnormal lymph nodes in the inguinal area.

the lower extremities, dermal backflow indicating various degrees of obstruction and, in one case, a tortuous dilated thoracic duct with almost total absence of lymph nodes in the inguinal area, pelvis, and retroperitoneal area.[13] Often patients have no gastrointestinal symptoms when they first present with hypoproteinemia and edema. Many have manifest mild diarrhea and steatorrhea.[13] Intestinal series show mucosal edema.[16,17]

The localized lymphangioma, *e.g.*, in an extremity, is easily controlled by excision, the most striking example being a cystic hygroma. As the tumor becomes more diffuse, it becomes more difficult to control with surgery. Finally, involvement of intestinal lymphatics must be treated supportively since no definitive method is known.

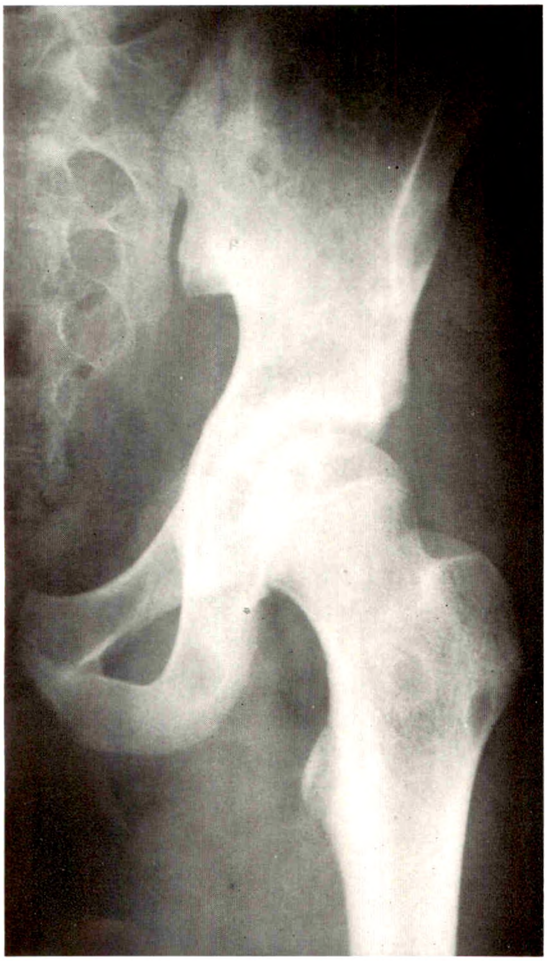


Fig. 19. Case viii. A roentgenogram showed cystic lesions in bone.

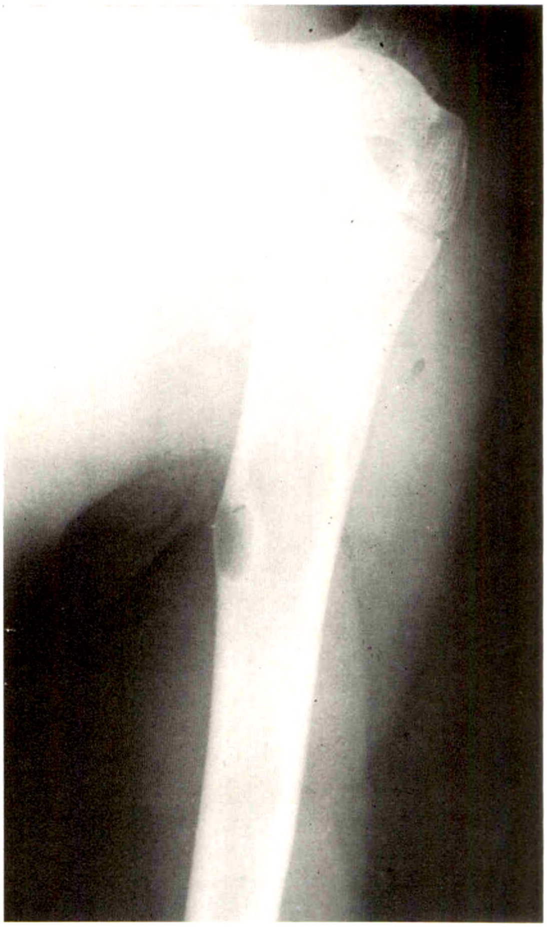


Fig. 20. Case viii. Multiple lytic lesions of bone due to lymphangiomata have been reported. Histologically, the defects are produced by pressure atrophy caused by dilated lymph channels.

SUMMARY

Eight patients with lymphangioma are reported to illustrate the broad range of potential involvement. Prognosis necessarily depends on the site of origin and the magnitude of tumor tissue present.

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RARE TUMORS IN CHILDREN*

By YAHYA M. BERKMEN, M.D.†
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NEOPLASMS of infancy and childhood are an interesting and commonly encountered pediatric problem. There has been an apparent increase in the over-all percentage of neoplasms in this age group in recent years, partially because of better and earlier diagnostic means and partially due to the decrease of death rate in early ages from infectious diseases, congenital malformations, etc. About 20 years ago malignancies were not even listed among the 10 most common causes of death, yet today they are considered third.[2]

Tumors of infancy and childhood, in general, show a marked difference in type, location, natural history and prognosis in comparison with those seen in adults. The benign tumors constitute the larger percentage of all neoplasms. Among malignant neoplasms sarcomas are 9 times more common than carcinomas, the reverse being true for adults. In Steiner's[44] series from this hospital consisting of 600 surgical specimens removed for diagnosis and treatment, about 22 per cent were malignant, 63 per cent were benign and 15 per cent were non-neoplastic lesions.

The most common types of benign tumors were of epithelial origin, such as polyps, papillomas and polypoid adenomas, followed by hemangiomas, dermoids and epidermoids, fibromas, lymphangiomas, nevi, teratomas, neurofibromas, lipofibromas, chondromas and osteochondromas.

Accordingto Dargeon,[15] the areas of the body most commonly involved with malignancies are: the bones, the kidneys, the eye and orbit, the lymphatic and blood forming organs, the soft somatic tissues and the nervous system. However, a classification of these sites according to the frequency of involvement cannot be made because, as pointed out by Andersen[1] "most of the statistics concerning childhood cancer suffer from the fact that the special interest of the hospital or of the other hospitals in the area are not taken into consideration."

The types of tumors encountered in children are very rarely seen after maturity, although they have been described in the adult.[15] On the other hand tumors in the adult are extremely rare in children. Cancer of the breast, uterus and ovaries in the female and cancer of the stomach, intestines and prostate in the male are very infrequent. However, the rare types do occur and familiarity by the radiologist with these unusual cases may help in making a correct diagnosis.

We reviewed the surgical pathology material of our hospital from 1949 through 1959 and, among more than 600 cases of benign and malignant tumors of infants and children, collected 7 rare neoplasms. Because of the extreme rarity of these tumors in children, no one has had much experience with them. Therefore, we felt it worthwhile to report our patients, in order to add a few cases to the scanty literature on this subject.

REPORT OF CASES

UNDIFFERENTIATED CARCINOMA OF THE SKIN

Case 1. The patient was 2½ months old when admitted to the Children's Memorial Hospital. He had a small tumor removed from the skin of the abdominal wall at the right lower quadrant in another hospital. This was not present at birth, but appeared later on and was noticed by his mother while bathing the baby.

After removal of this tumor from the abdominal wall, a similar small tumor became evident at the angle of the mouth on the left side. Biopsy taken from this growth revealed an undifferentiated carcinoma. The slides of the tumor removed from the abdominal wall were reviewed and they showed an identical

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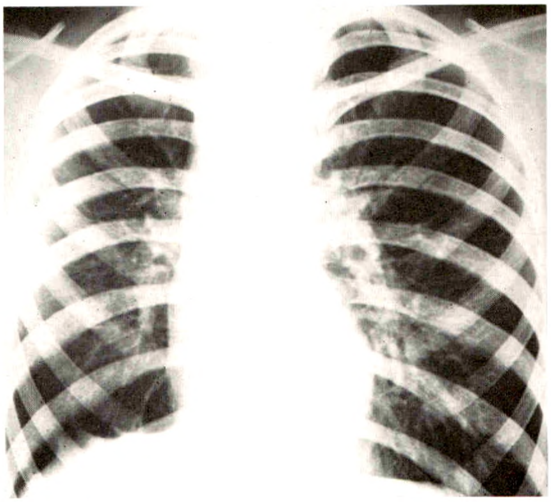

Fig. 1. Case III. Bronchial adenoma. Chest roentgenogram on admission shows right upper lobe atelectasis.

type of carcinoma. No radiation therapy was given at this time. The patient was lost to follow-up.

EPIDERMOID CARCINOMA OF THE TONGUE

Case II. Although this case has been reported elsewhere by Merrifield, Dalitsch and Steiner,[31] for the convenience of the reader, a brief summary of the case is given. This 5 year old female child had an oral tumor on the left side of the tongue with extension into the floor of the mouth. The tumor was removed, but it recurred and progressed rather rapidly. Three months later a complete surgical removal was unsuccessfully attempted. The biopsy confirmed the diagnosis of epidermoid carcinoma. In a short period of time, metastasis to the left cervical lymph nodes occurred and extended to the opposite site. Radiation therapy could not delay a fast downhill course and the child died 8 months after the first surgery.

Comment. Carcinomas, in general, are very rare in children. As stated earlier, 10 per cent of all malignancies in children are carcinomas in contrast with 90 per cent sarcomas. Among this small percentage of carcinomatous malignancies, those involving the skin, buccal mucosa, tongue, mastoids, etc. are even more infrequent. According to the statistics of the California Tumor Registry, only 0.4 per cent of the malignant skin tumors occur in persons under 15 years of age.[43] Saleeby[38] could find only 8 cases of cancer of the tongue in children reported in the literature and added 1 of his own. From 400 cases of malignant tumors of the paranasal sinuses seen at Mayo Clinic, only 4 were under 14 years of age; the youngest was 5 years old.[4]

These figures reflect the rarity of this condition; however, they also show the importance of taking a biopsy of any suspicious lesion, in order to institute the proper diagnosis and therapy. Although the majority of cancers of the oral cavity end fatally, long term cures are also described, as the patient of New and Hertz[33] who was well 16 years after therapy for a lower lip squamous cell carcinoma.

BRONCHIAL ADENOMA

Case III. This $9\frac{1}{2}$ year old female was admitted to the Children's Memorial Hospital with right lobe atelectasis (Fig. 1). Her past history was noncontributory until about 6 months before admission when she had a coughing spell, hemoptysis and showed a weight loss of 6 pounds. At the beginning of her symptoms the chest roentgenogram demonstrated changes which were interpreted as viral pneumonitis. Another chest roentgenogram was taken 2 months later with a mobile unit and a work-up for tuberculosis was suggested. However, 2 consecutive skin tests were negative.

One month before admission, right upper lobe atelectasis was noted and she was referred to this hospital for further evaluation.

The physical findings on admission were confined to the chest. There were diminished breath sounds and expansion, increased fremitus on the right side and apical dullness on percussion.

Bronchoscopy showed a tumor mass at the carina in the right main bronchus. Because of massive bleeding, the tumor could not be removed at this time, but partial removal of the tumor was possible at the time of a second bronchoscopy. Microscopic examination of the biopsy specimen revealed bronchial adenoma.

She remained asymptomatic after the procedure. However, several bronchoscopies were necessary for cauterization and removal of the residuum of the tumor.

She was in good health when seen $5\frac{1}{2}$ years after the first excision.

Case iv. This $12\frac{1}{2}$ year old male was admitted to the Children's Memorial Hospital following bouts of fever, chills, cough and grayish expectoration for about 8 months. A bronchogram made elsewhere was said to show bronchiectasis. The chest roentgenogram on admission demonstrated atelectasis of the right middle lobe (Fig. 2).

Bronchoscopy performed after admission disclosed a large, granulomatous, friable and easily bleeding mass in the apical segment of the right lower lobe bronchus. The biopsy revealed bronchial adenoma.

Lobectomy was decided upon. On exploration of the chest, the middle and lower lobes were found to be bound together with dense, inseparable adhesions. Both lobes were resected.

Microscopically, the tumor appeared to be invading the bronchial wall and in some areas it was seen outside the cartilage surrounding the bronchus. No mitotic figures were seen. The sections taken from one of the lymph nodes revealed poorly differentiated tumor cells in the small areas.

In most areas the tumor was covered with stratified squamous epithelium; however, in other places pseudostratified epithelium with no apparent cilia was noted. The microscopic diagnosis was cylindroma.

The patient is well and without recurrence 7 years after the surgery.

Comment. Although benign tumors of the upper respiratory tract, *i.e.*, laryngeal polyps or papillomas, are quite frequent in infancy, tumors of the bronchus are extremely rare in early ages and childhood. Tumors arising from the bronchus are mainly bronchogenic carcinomas and bronchial adenomas. Rare occurrence of the bronchogenic carcinoma in infancy and childhood is reported in the literature.[10,22]

Bronchial adenomas in children show characteristics identical as far as location, histologic appearance and symptomatology are concerned to those of adults. These well known features of the bronchial adenomas will not be repeated here.

Most of the reported cases of bronchial adenomas in children occurred between the age of 9 and 13 years.[21,37,42] However, it has been encountered at as early an age as 4 years.[6]

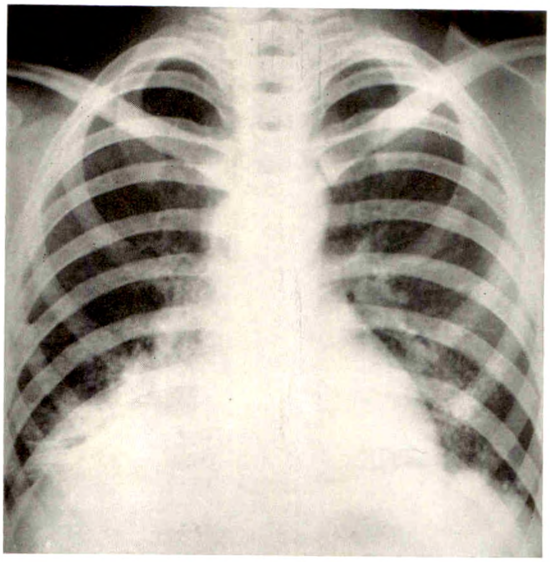

Fig. 2. Case iv. Bronchial adenoma. Chest roentgenogram on admission shows atelectasis of the right middle lobe.

Though these tumors can be removed with the aid of bronchoscopy, total excision may not be possible in all cases and repeated excisions and fulgurations may be necessary because of local recurrences, as in our Case iii. One should keep in mind the possibility of malignant degeneration of the tumor. Furthermore, on planning the treatment, one should realize that most of these tumors have an extrabronchial as well as intrabronchial part, thus making lobectomy or pneumonectomy necessary.[3]

PERICARDIAL MESOTHELIOMA

Case v. This 2 year old female suddenly developed dyspnea and cough. Four days later she was admitted to another hospital because of progressing symptoms. The roentgenogram of the chest showed a mediastinal mass and collapse of the second lumbar vertebra. She was transferred to the Children's Memorial Hospital for further work-up, 8 days after the onset of the first symptoms.

On admission she was cyanotic and dyspneic. The liver was palpated 2 fingerbreadths down from the right costal margin and the neck veins were distended. There was dullness over the

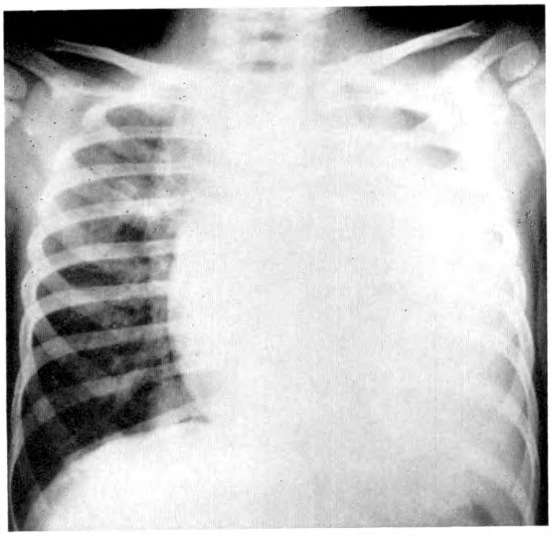

FIG. 3. Case v. Pericardial mesothelioma. Chest roentgenogram on admission shows a large mediastinal mass which cannot be separated from the cardiac shadow. The mass involves the upper mediastinum as well and extends into the left hemithorax, leaving only a small aerated lung field visible.

entire left chest and bronchophony of the left back. No murmurs were heard.

Roentgen examination confirmed the presence of the mediastinal mass (Fig. 3) and the compression of the second lumbar vertebra.

Five days after the admission, exploration of the chest under general anesthesia was done. After opening the pericardial sac, an irregular nodular tumor mass was discovered. Tumor was also found over the right ventricle to such an extent that the pulsations of the ventricle were not visible. Numerous similar masses were present, scattered over the lung parenchyma. The left lung was completely atelectatic. The mediastinum was thick and completely replaced by tumor.

Histologic diagnosis of the biopsy was embryonal sarcoma.

The patient received nitrogen mustard therapy on the fifth postoperative day. One week after therapy, the metastatic nodule in the chest disappeared and the mediastinum became smaller.

One month after nitrogen mustard therapy, she was re-admitted because of cardiac failure and dyspnea. Pain was present in both knees. Metastatic involvement of the distal end of the right femur, the right humerus, and L-4 and L-5 was demonstrated on roentgenograms. She rapidly deteriorated with evidence of increasing mediastinal pressure and expired 3 months after the operation.

The autopsy confirmed the findings of pericardial sarcoma invading the mediastinum, heart and lungs, with distant metastases to the skin, vertebrae and the right ovary.

Comment. Pericardial tumors are classified and studied together with the cardiac tumors because of their close anatomic, clinical and pathologic association. In general, tumors arising primarily from the pericardium are very rare. When primary and secondary tumors of the heart and the pericardium are considered together, it is seen that metastatic tumors from the lung, from the mediastinum by invasion or from distant organs by hematogenous or lymphatic spread are the commonest type of malignancy. This is followed in the order of frequency by primary tumors of the heart. Primary tumors of the pericardium are the least common.[45]

In a period of 20 years 11,100 consecutive autopsies were performed at the Cleveland City Hospital, 1,082 of which were on patients who expired of malignant diseases. One hundred and eighteen of these 1,082 cases showed secondary involvement of the heart and pericardium (10.9 per cent). Most of the primary lesions were in the breast and bronchus and accounted for 48 per cent of the cases in this series.[41] Lymburner, as cited by Parker *et al.*,[35] in a review of 8,550 necropsies, found 4 cases of primary tumor of the heart and 52 cases of secondary metastatic lesions of the heart.

Of all the primary tumors of the heart, the majority are benign, malignant tumors constituting only 25 per cent of the total.[35] The discussion of the cardiac tumors is beyond our scope. The interested reader can find a number of excellent reviews of the subject in the literature.[7,17,28,35,36]

The pericardium is composed of fibrous connective tissue traversed by vessels, lymphatics, nerves and mesothelium covering from both surfaces. Therefore, both benign and malignant lesions may originate from either of these tissues. Benign tumors of the pericardium can be removed surgically with complete cure and regression of the cardiac symptoms. Examples of the surgical removal in children of benign tumors of the pericardium, such as intrapericardial teratoma,[5] cavernous hemangioma,[24] lipoma,[29] bronchogenic cysts,[14,40] pleuropericardial cysts and lymphangiomas,[14] are recorded in the literature.

The malignant tumors are mostly fibrosarcomas, various angiosarcomas, lymphosarcomas, liposarcomas, neurogenic sarcomas and mesotheliomas, the latter being most common.[11]

There has been considerable discussion about the authenticity of the pericardial tumors arising from the mesothelial lining. Although their existence has been questioned, even denied by some,[47] today it is a general belief that they do exist as a definite pathologic entity.[16,39,45] The terms of mesothelioma, celiothelioma, endothelioma, endothelial carcinoma, pericardial carcinoma are used in the literature for these tumors, either interchangeably or in close synonymity.[16,39]

It is said that malignant mesotheliomas produce polyarthritis as do their pleural counterparts,[11] and the pericardial fluid in these cases contains hyaluronic acid; as yet, its significance and value in the differential diagnosis remains to be determined.[25]

It seems that primary malignant tumors of the pericardium are predominantly found in the young adults, and males are more often affected than females.[45] Apparently, these lesions occur with extreme rarity in children. In our review of the literature, we could find but one case, reported by French authors,[25] concerning a 13 year old boy who succumbed to malignant pericardial tumor which was diagnosed as a fibroblastic mesothelioma. Therefore, we believe that our case is the youngest patient with malignant mesothelioma ever recorded.

SARCOMA OF THE STOMACH

Case vi. This 5 year old female child was admitted on August 17, 1958 to the Children's Memorial Hospital with a history of intermittent fever, anorexia and anemia since May, 1958. Physical examination was normal. Skin tests for tuberculosis were negative, as well as serology, numerous lupus erythematosus preparations and bone marrow aspiration. She was discharged with a presumptive diagnosis of leukemia. Twenty milligrams of medrol were given daily. The medication was gradually decreased. She did well under this regimen until 2 weeks prior to the second admission when she developed chills, fever and sweating and was readmitted on February 16, 1959.

Again the physical examination was negative. Her hemoglobin was 9.5 gm. per cent. She had occult blood in her stools and the hemoglobin dropped to 7.1 gm. per cent. No further investigation was done and she was discharged, only to be admitted again on May 13, 1959 because of continued occult blood. This time the liver was palpable 2 cm. below the right costal margin and there was fluid in the abdomen. Proctoscopy was negative. No neoplastic cells were found in the gastric secretions. An upper gastrointestinal series showed a polypoid mass in the fundus of the stomach with marked distortion of the mucosa (Fig. 4, *A* and *B*).

Surgical exploration on May 14, 1959 revealed a hard mass within the fundus infiltrating the wall of the stomach and protruding into the lumen with extension to the lower esophagus. Frozen section of the biospy revealed sarcoma, and a partial gastric resection, excision of the lower esophagus with a portion of the left diaphragm and splenectomy were performed.

Postoperatively, intravenous nitrogen mustard (0.2 mg./kg.) and small doses of conventional roentgen-ray therapy to the abdomen were given. She was discharged on the 19th postoperative day to receive additional roentgen-ray therapy elsewhere.

Her final admission was on November 24, 1959. She had low grade fever and purulent expectoration. Chest roentgenograms showed enlargement of the upper mediastinum, obviously due to metastasis to the lymph nodes. There was an extrinsic pressure at the greater curvature of the stomach which was thought to be due to the enlarged mesenteric lymph nodes

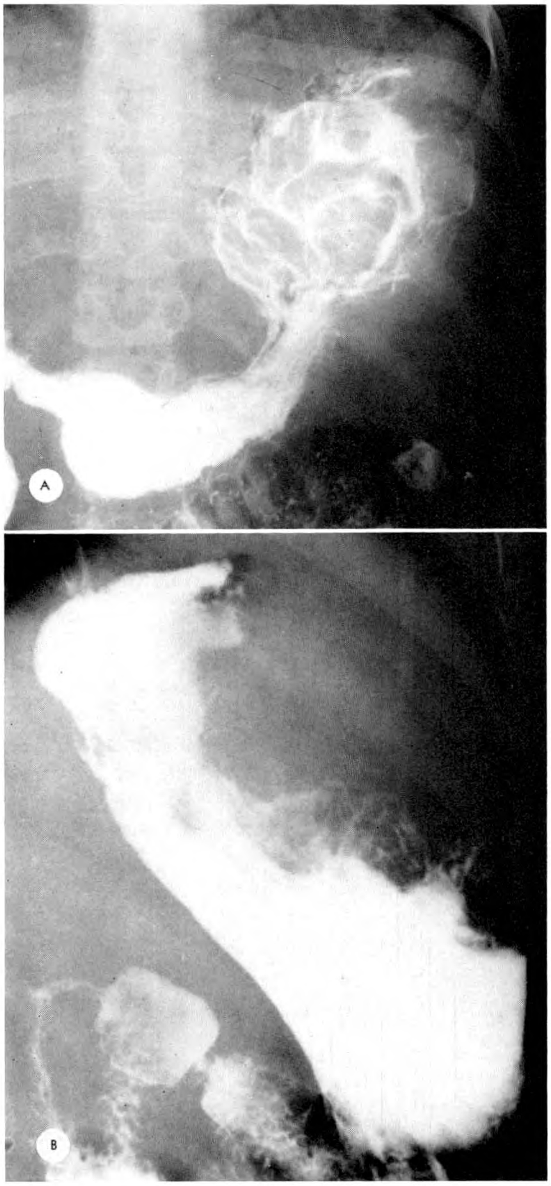

FIG. 4. Case VI. (*A* and *B*) Sarcoma of the stomach. An irregular, large mass in the fundus, extending posteriorly into the body, is demonstrated. There is marked distortion of the gastric mucosa.

and/or metastatic extension to the mesentery.

She was sent home and was followed by her family physician who reported that she had anorexia and vomiting. A large mass appeared in the epigastrium extending to the umbilicus. She expired at home on December 15, 1959, approximately 1 month after her final discharge. No autopsy was performed.

Comment. Tumors of the stomach, either benign or malignant, are extremely rare in infancy and childhood. Dargeon[14] found only 1 case of leiomyosarcoma, occurring in a 10 year old boy, in the files of the Children's Tumor Registry of Memorial Center. Among the benign tumors, leiomyomas and ectopic pancreatic tissues are the most common lesions in this age group.[26] Others, such as tridermal teratoma, gastric polyposis as a manifestation of Peutz-Jeghers syndrome and neurofibromatosis, also have been reported.[27,46]

Malignant lymphomas, carcinomas and sarcomas of the stomach are encountered in children. A very rare occurrence of primary neuroblastoma of the stomach is also recorded.[27]

Goldstein[18] made a very extensive review of all available literature of the world and collected approximately 350 instances of primary malignancy of the stomach and intestines in children and young adults under 25 years of age. Based on the number of cases cited by him, carcinoma of the stomach outnumbers gastric sarcoma.

Carcinomas in children most commonly involve the antral portion of the stomach and are most probably of mucous gland origin.[27] Carcinoma of the fundus with perforation is also reported.[19]

In the sarcomatous group of malignancies, leiomyosarcomas, rhabdomyosarcomas and lymphosarcomas are the most expected types. In Goldstein's collected cases, the youngest patient with sarcoma was 3 years and 9 months of age.[18]

The clinical diagnosis of gastric malignancies is very difficult. This is partially because of the rarity of the condition. The prominent symptoms are loss of appetite, vomiting, eructations and an enlarged abdomen. Pain is rare and emaciation is usually absent because of the rapid growth of the tumor.[19]

The outcome is usually fatal with metastases to the liver, peritoneum and mediastinum. Few survivals of gastric carcinoma and sarcoma cases are known. Hale and Mallo[20] reported a case of a 16 year old female with infiltrating ulcerative immature papillary adenocarcinoma which metastasized to the mesenteric lymph nodes. Total gastrectomy and splenectomy were done and she was well 6 years after the operation. Also the survival of $2\frac{1}{2}$ and $3\frac{1}{2}$ year old children, both females, with leiomyosarcoma of the stomach is mentioned by Landing and Martin.[27]

In the roentgenographic differential diagnosis of gastric sarcomas, bezoars, hematoma of the gastric wall, Menetrier's[26] and Crohn's[32] diseases should be considered.

SARCOMA OF THE URINARY BLADDER

Case vii. This 1 year and 10 month old male infant was admitted to the Children's Memorial Hospital with a history of dysuria, tenesmus and difficulty in starting urination for a period of 6 weeks. He was treated elsewhere for urinary tract infection with an unknown antibiotic and circumcision was also done.

On admission, the physical examination revealed nothing unusual. The urine showed microscopic hematuria. An intravenous pyelogram demonstrated normal kidneys, but a filling defect at the base of the bladder was visualized (Fig. 5). Suprapubic cystostomy and electro-resection plus fulguration were done.

The tumor increased in size and 3 months after operation roentgen-ray therapy was given without benefit. Six months after the operation a ureterosigmoidostomy was performed and this was followed by total cystectomy and prostatectomy.

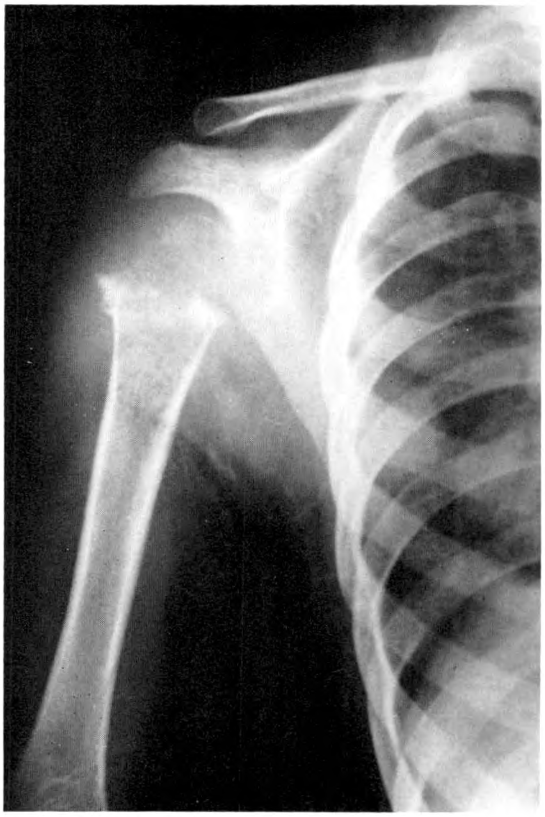

Fig. 6. Case vii. Same patient as in Figure 5. Roentgenogram shows metastasis to the right humerus. Two fairly large metastatic nodules are seen within the right lung.

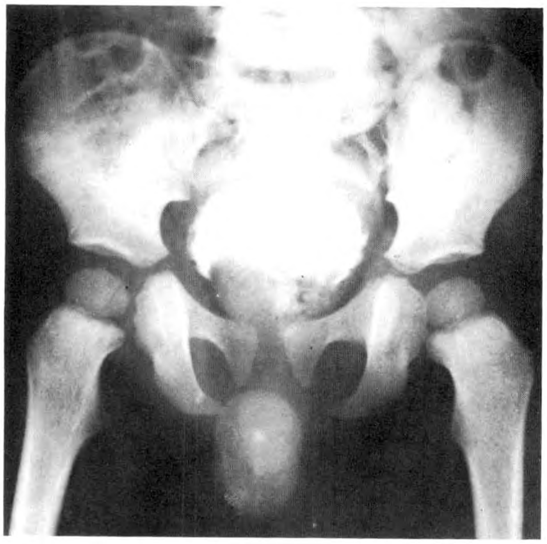

Fig. 5. Case vii. Sarcoma of the urinary bladder. There is a large, irregular and somewhat lobulated filling defect of the urinary bladder. There is trabeculation of the bladder wall.

Terminally, metastases to the right humerus (Fig. 6), both distal femora and chest developed.

The child died 10 months after the first operation. No autopsy was obtained.

Microscopic examination of the surgical specimens revealed rhabdomyosarcoma of the bladder.

Comment. Sarcomas of the urinary bladder are generally rare in all ages. Only a few are recorded in every large series of malignant tumors. It appears that bladder sarcomas are usually seen in very young or very old persons. In children, half of the reported cases were under 2 years of age.[9]

Almost all malignancies of the urinary

bladder are sarcomas—carcinomas being extremely rare. It is also said that exstrophic bladder has predisposition for adenocarcinomas. McIntosh and Worley[30] found 40 such cases, but the youngest of these patients was 21 years old.

Rhabdomyosarcomas and myxosarcomas are the commonest types.[12] However, leiomyosarcomas, angiosarcoma, chondrosarcoma[23] and primary osteogenic sarcoma[34] of the bladder are also reported.

These are fast growing tumors with infiltration and invasion of the neighboring tissues. Therefore, when first seen, cystoscopically or at surgery, the exact origin of the tumor cannot be determined. Histologic differentiation may frequently be made, but many cases still cannot be definitely classified as far as the origin is concerned.[8] Danckers *et al.*[13] proposed to group such cases together as "sarcomas of the bladder neck, prostate and periprostatic tissues."

The prognosis is very poor and these children die in a short time with metastases and urinary tract obstruction leading to infection and renal failure. Danckers *et al.*[13] found 5 cases of survival reported in the literature. Dargeon[14] mentions 2 other cases of sarcoma botryoides of the bladder with 6 years of survival. Hence, it seems worthy to use every effort in treating these children (surgically and by roentgen-ray therapy), although most of the time the results are discouraging.

SUMMARY

Seven cases of rare tumors in children are reported. The importance of being familiar with rare tumors is emphasized and attention is called to the fact that, although the outcome in these cases is most often fatal, the literature contains several examples of long term survival and even apparent cure.

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THE ROENTGEN DIAGNOSIS OF ABDOMINAL MASSES IN CHILDREN*

INTRAVENOUS UROGRAPHY VS. INFERIOR VENACAVAGRAPHY

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THE roentgenographic approach to the diagnosis of abdominal masses has always depended heavily upon the urographic method.[4] In childhood, more masses occur in the kidney than in any other abdominal organ. The adrenal gland and allied components of the sympathetic system are the source of almost as many masses. The diagnosis of tumors of other tissues in a retroperitoneal location is frequently facilitated by the carrying out of intravenous urography.

Only recently has another roentgenographic method been found to be useful in the work-up of abdominal masses. Inferior venacavagrams have been determined to be helpful not only in arriving at a diagnosis but also in deciding upon method and course of therapy.[6]

TECHNIQUES

Evidence is accumulating to indicate that modern tri-iodinated contrast media may be injected in large doses without significant untoward sequelae.[11] In infants, it has in many centers become common practice to inject concentrated diatrizoate compounds (hypaque 50 per cent or renografin 60) in doses of 2 to 4 ml. per kg. body weight.[7,10]

The concentrating power of the kidney of a newborn child is less than that of an older child or adult. Because maximum osmolarity is approximately half the figure encountered in the urine of an adult,[8] the density of the contrast medium excreted by the kidney during the first few days of life is not very great. Furthermore, there is in any young infant a low degree of contrast between solid and gas-containing regions of the abdomen, and the intestinal gas pattern may render it very difficult to visualize the kidney collecting systems through the loops of bowel. For these reasons we avoid, whenever possible, carrying out intravenous urography during the first few weeks of life. If it is important to obtain information in the newborn period, however, we feel it justified to carry out an examination utilizing concentrated diatrizoate in a dose of 2 ml. per kg. (Fig. 1, *A* and *B*).

If the urogram does not produce sufficient delineation of the urinary tract and more information is required concerning abdominal organs, we do not hesitate to carry out inferior venacavagraphy. Visualization of the inferior vena cava may or may not in itself be important. In either case, the procedure is a good method of obtaining additional information concerning the urinary tract. A large needle (preferably 18 gauge) is inserted into a saphenous vein, and diatrizoate is injected. The intravenous administration of diatrizoate for inferior venacavagraphy is the same as for intravenous urography, except in 2 respects: (1) the injection is given as rapidly as possible, preferably within 3 seconds; and (2) two injections are made (providing a *total* dose of double that used in intravenous urography) and lateral and anteroposterior roentgenograms of the abdomen are taken *during* the injection. These two views constitute the inferior venacavagram. Following Hillman and Tristan's recommendation,[2] we expose the lateral film first. By the time we change the roentgenographic tube from lateral horizontal to

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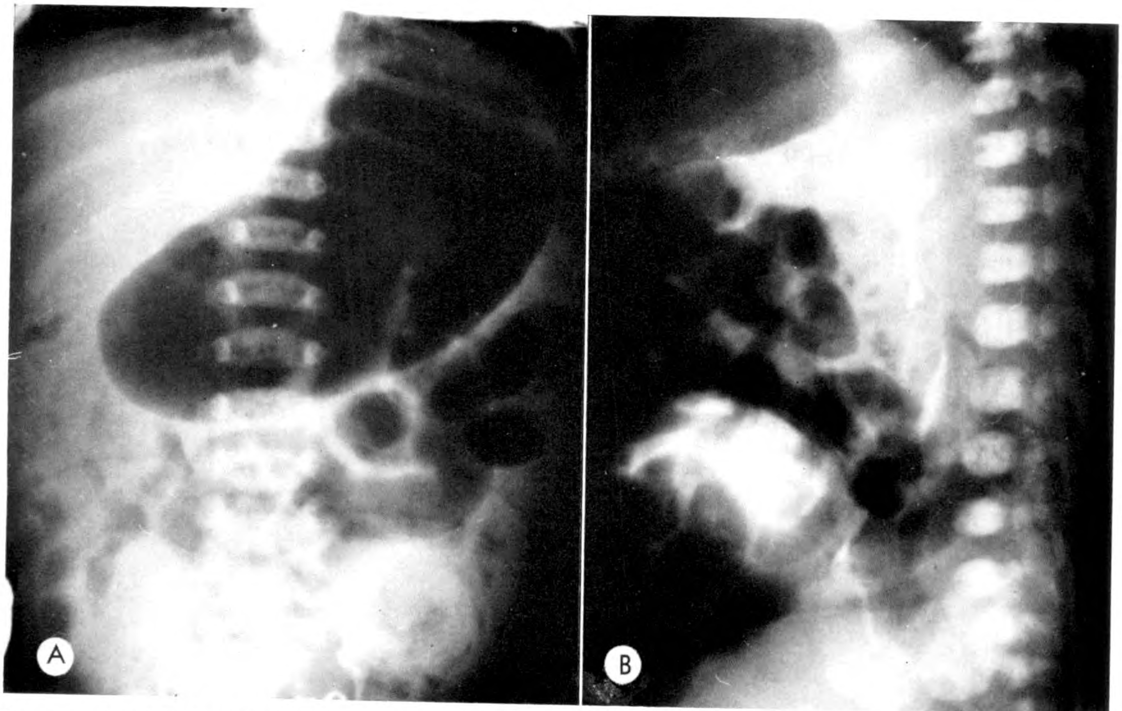

Fig. 1. (*A* and *B*) Intravenous urograms made at 3 days of age because of a right flank mass felt on physical examination in the newborn period. The right kidney is not clearly demarcated and does not excrete contrast material. The left kidney has a normal appearance. The baby was given ginger ale after the injection of contrast medium, and the roentgenograms show the stomach moderately distended with gas.

overhead position (without moving the patient from supine position), a minute or more has passed, and the anteroposterior roentgenogram includes a very satisfactory intravenous urogram (Fig. 2, *A* and *B*). Inferior venacavagraphy is thus a procedure which is supplementary to, not competitive with, intravenous urography.

Later roentgenograms may be obtained after the initial ones in the same fashion as ordinary urograms.

Such an approach was utilized in the investigation of an infant admitted for hyperbilirubinemia whose examination revealed a mass in the right flank and blood in the urine. Inasmuch as the intravenous urogram was inconclusive regarding an abnormality of the right kidney (Fig. 3, *A* and *B*) and a Wilms' tumor remained a distinct possibility, inferior venacavagraphy was carried out. The latter procedure showed no deflection of the inferior vena cava from its normal course, but did more clearly delineate a deformity of the superior calyx of the right kidney (Fig. 4, *A* and *B*). The patient's blood loss was thought to be due to a retroperitoneal hematoma, and was treated by transfusion. The right upper quadrant mass gradually became less prominent to palpation. A follow-up intravenous urogram 4 months later showed the restoration of a normal position and calyceal pattern in the right kidney.

EVALUATION OF OPERABILITY

Another way in which information obtained by inferior venacavagraphy supplements that acquired by intravenous urography is in the area of evaluation for therapy. Abdominal tumors, in general, are best managed primarily by surgery, both for pathologic diagnosis and definitive treatment. Nevertheless, it is very helpful to the surgeon to know as much as possible about the nature of a given mass before he approaches it directly. Inferior venacavagraphy provides one additional piece of information concerning resectability. A tumor in a patient whose inferior vena cava is blocked is not likely to be readily resectable, and the presence of such a block is an indication for the preoperative administration of radiation therapy to the tumor.

Such a course was followed in the case shown in Figures 5, *A* and *B*; and 6, *A* and *B*. After a central tumor dose of 2,300 rads was administered to the tumor by 2 mev. therapy and actinomycin D had been given intravenously, the patient was explored. The kidney with its tumor was removed and was found to be a mesoblastic Wilms' tumor. The inferior vena cava was filled with tumor thrombus which had invaded from the left renal vein. This tumor thrombus was extracted. A follow-up inferior venacavagram one year later showed no evidence of recurrence of tumor in the vena cava. The child has remained clinically free of tumor $1\frac{1}{2}$ years.

An example of a tumor showing no vena cava involvement is shown in Figures 7, *A* and *B*; and 8, *A* and *B*.

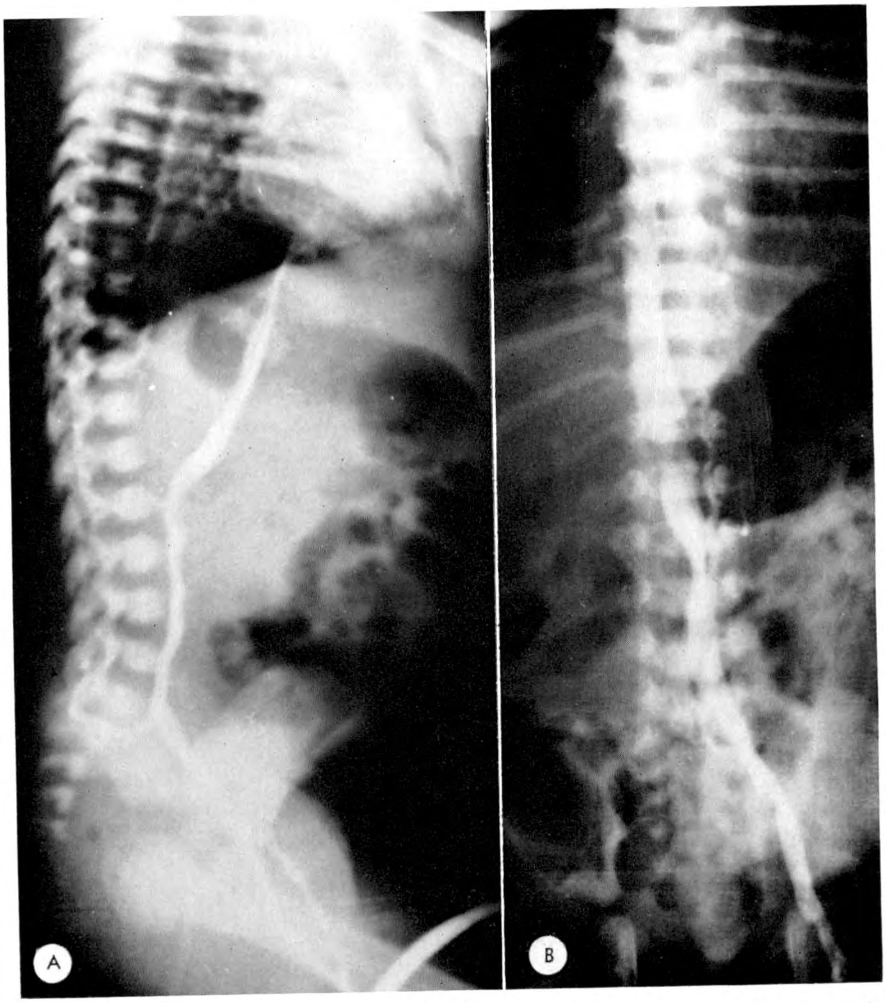

FIG. 2. (*A* and *B*) Normal inferior venacavagrams of the same patient shown in Figure 1, *A* and *B*. Both views reveal passage of contrast medium into lumbar collaterals and thence into the azygos system as well as delineating the direct course of the inferior vena cava. The anteroposterior study again depicts excretion by a left kidney, none by the right. Laparotomy revealed a large multicystic right kidney, which was removed. The right ureter was atretic, and there was no drainage path for the abnormal kidney.

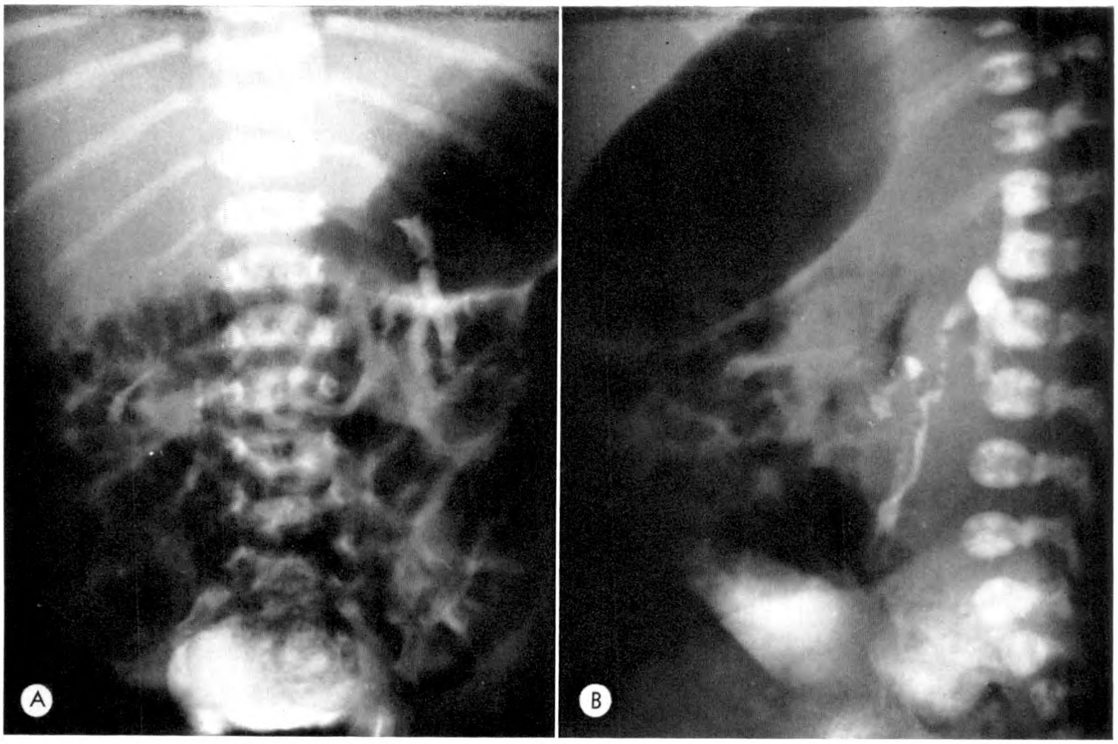

FIG. 3. (*A* and *B*) Intravenous urograms at 8 days clearly delineate the collecting system of the left kidney but not of the right.

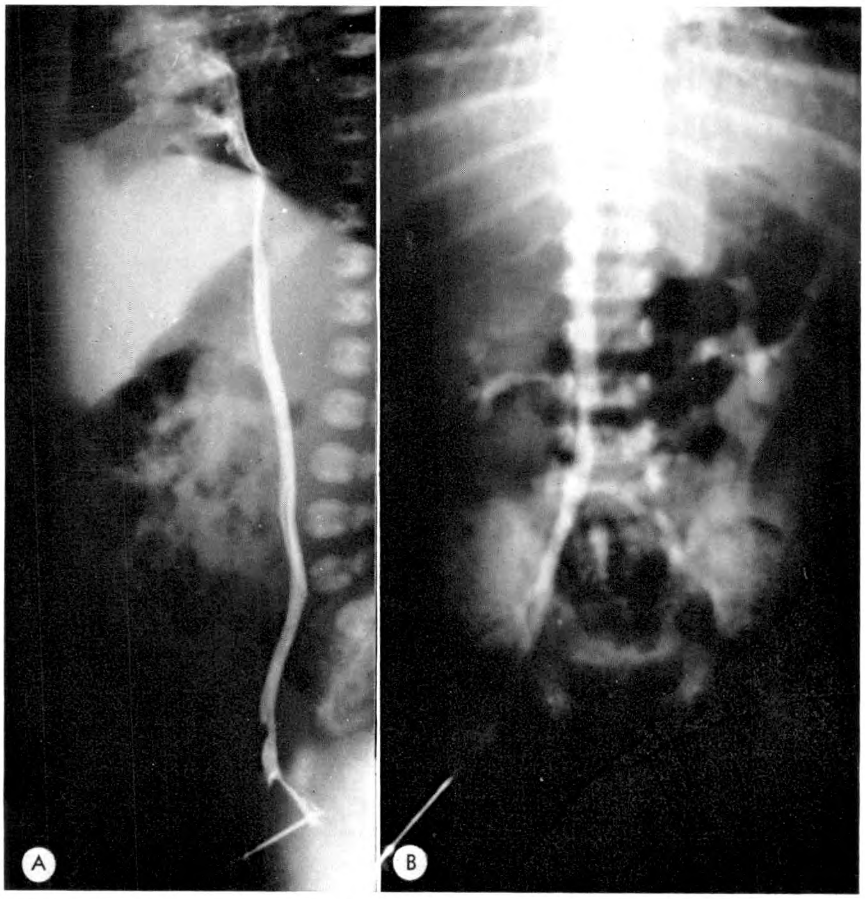

FIG. 4. (*A* and *B*) Inferior venacavagrams of the same patient shown in Figure 3, *A* and *B*, at 12 days reveal a normal course of the inferior vena cava. The examination better demonstrates caudal displacement of the right kidney, with irregularity of the superior calyx and flattening of the upper pole, than did intravenous urography.

ASSESSMENT OF INFERIOR VENACAVAGRAMS

Filling of the ascending lumbar veins via collateral communications of the inferior vena cava frequently makes it difficult to ascertain whether the inferior vena cava is occluded or not. We carry out the procedure without anesthetizing the patient, which means that he is probably crying or straining rather than lying submissively on the roentgenographic table. It is very easy for him thus to increase his abdominal pressure to the point where blood (and contrast medium) does not flow into the inferior vena cava but passes into the lumbar veins. Such, we suspected, was the situation in Figure 9, *A* and *B*, which shows the inferior venacavagram in a child with a huge right abdominal mass. The right common iliac vein was displaced into a Z course, but showed a fairly large lumen on the anteroposterior roentgenogram.

Not only did the examination make a decision as to operability difficult, it also presented us with a dilemma as to the nature of the tumor. It is practically axiomatic that neither Wilms' tumors nor neuroblastomas cause a kidney to be completely nonfunctioning. Yet, neither on our inferior venacavagram nor on our follow-up urogram could we see any evidence of excretion by a right kidney (Fig. 10, *A* and *B*).

Laparotomy revealed a huge unresectable right abdominal mass extending across

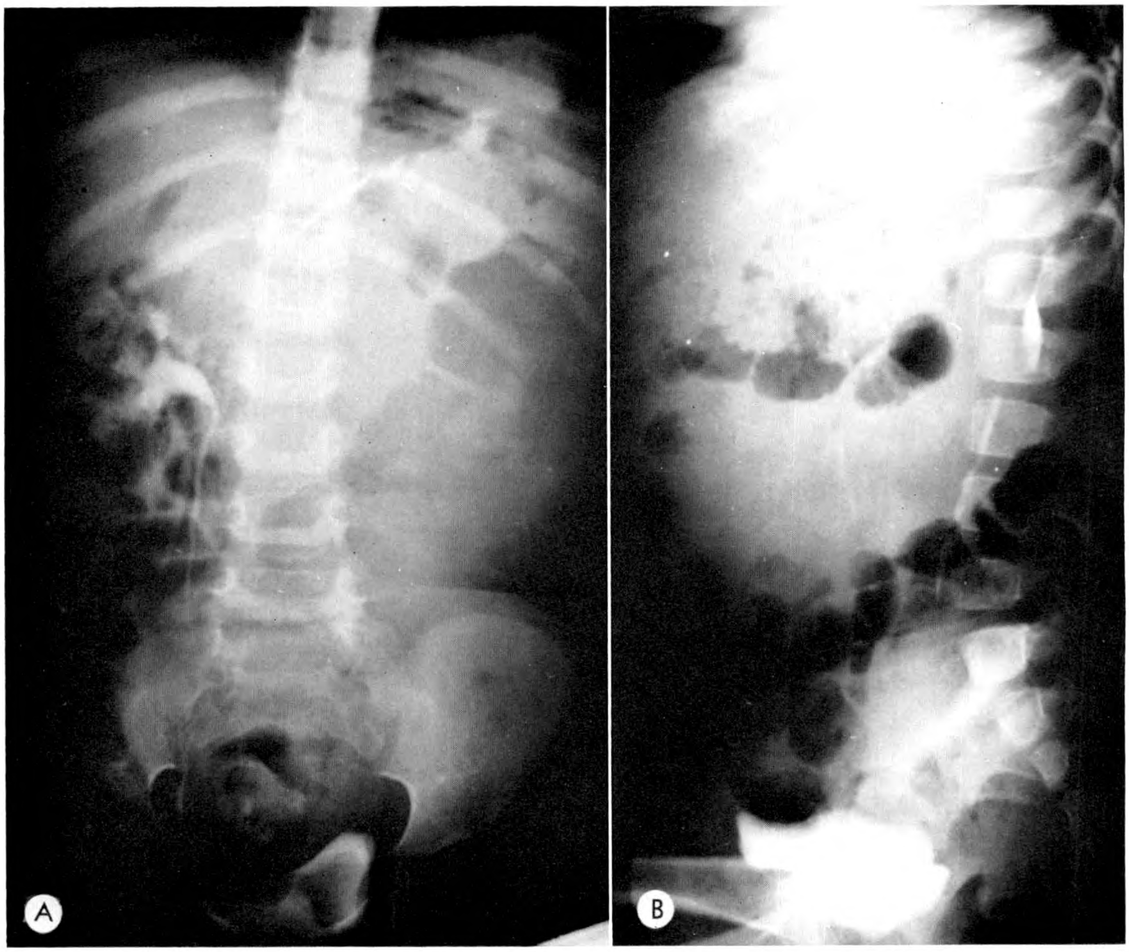

FIG. 5. (*A* and *B*) Intravenous urograms of a 3 year old girl admitted because of hematuria. On physical examination a large firm mass was readily palpable in the left side of the abdomen.

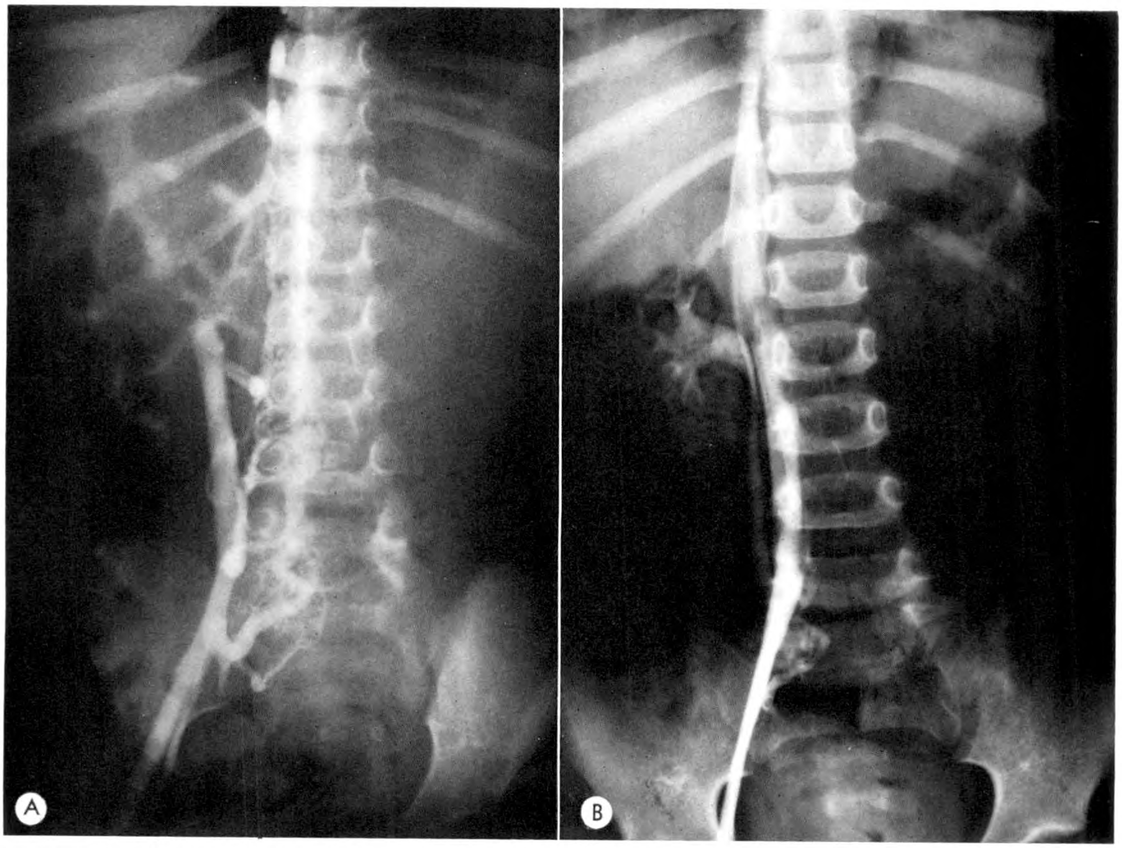

FIG. 6. (*A* and *B*) Inferior venacavagrams of the patient shown in Figure 5, *A* and *B*. *A*, made 3 days after intravenous urography, shows displacement of the inferior vena cava by the tumor mass and complete obstruction at the level of the second lumbar vertebra. Supervoltage radiation therapy and actinomycin D were administered. The tumor was removed 17 days later, at which time a tumor thrombus filled the inferior vena cava and was also removed. *B* shows a follow-up study 1 year after surgery. There was no clinical or roentgenographic evidence of tumor present.

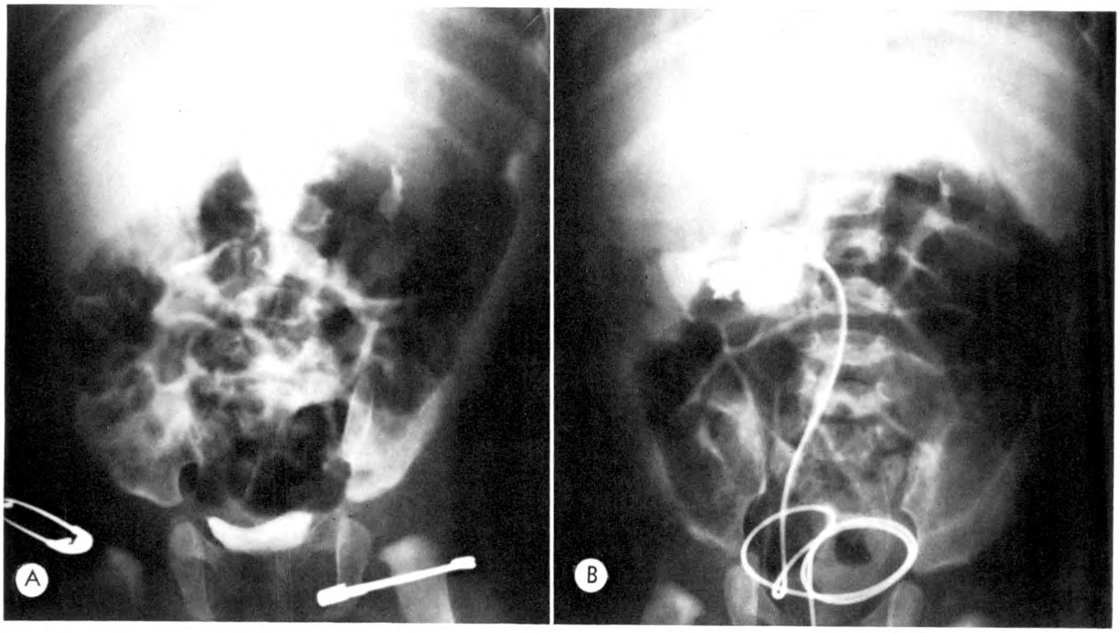

FIG. 7. (*A* and *B*) Urograms of a 5 month asymptomatic female in whom a large right abdominal mass was felt on routine physical examination by the child's pediatrician. The right kidney is displaced caudad, but it is uncertain whether the tumor arises in the adrenal or the liver.

the midline and involving the lymph nodes about the inferior vena cava and aorta. The patient was treated with supervoltage irradiation to a tumor dose of 2,500 rads and 5-fluorouracil, without beneficial response. Five weeks after surgery she died. Autopsy disclosed the tumor to be a highly anaplastic carcinoma, perhaps having originated in the adrenal, which involved the kidney and the liver. The tumor obstructed the right ureter but only narrowed and did not occlude the inferior vena cava.

Another patient was transferred to Babies and Childrens Hospital at the age of 2 days because of a tremendous right abdominal mass. Venacavagrams showed no filling of the inferior vena cava, only collateral flow through the lumbar system (Fig. 11, *A* and *B*). The anteroposterior roentgenogram also revealed much greater opacification of the left than the right side of the abdomen, suggesting that the mass in the right side was largely avascular. Urograms (Fig. 11, *C* and *D*) following the inferior venacavagraphy confirmed this impression and revealed the right kidney to be functioning well although displaced into the left side of the abdomen.

Obviously, the mass arose from a retroperitoneal location. It was our impression that the inferior vena cava likely was not visualized, not so much because of occlusion, but simply because of mechanical pressure by the huge tumor. Our thoughts were confirmed at laparotomy, at which the inferior vena cava lumen was found to be compressed but not blocked. The mass appeared cystic and was attached to the caudate lobe of the liver, immediately beneath the right hemidiaphragm, but had

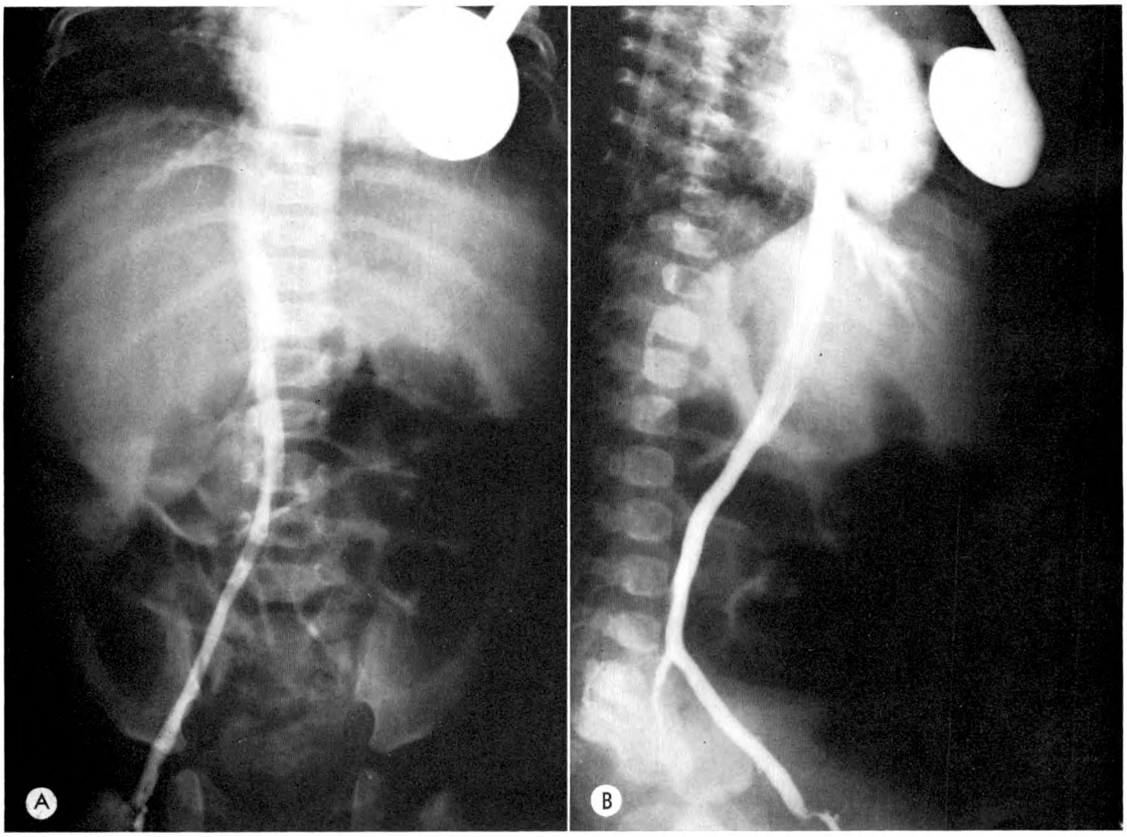

Fig. 8. (*A* and *B*) Inferior venacavagrams of the same patient shown in Figure 7, *A* and *B*. There is slight deflection of the course of the inferior vena cava by the right upper quadrant mass, but no evidence of invasion of its lumen. At operation, a large neuroblastoma involving the right lobe of the liver was found and removed.

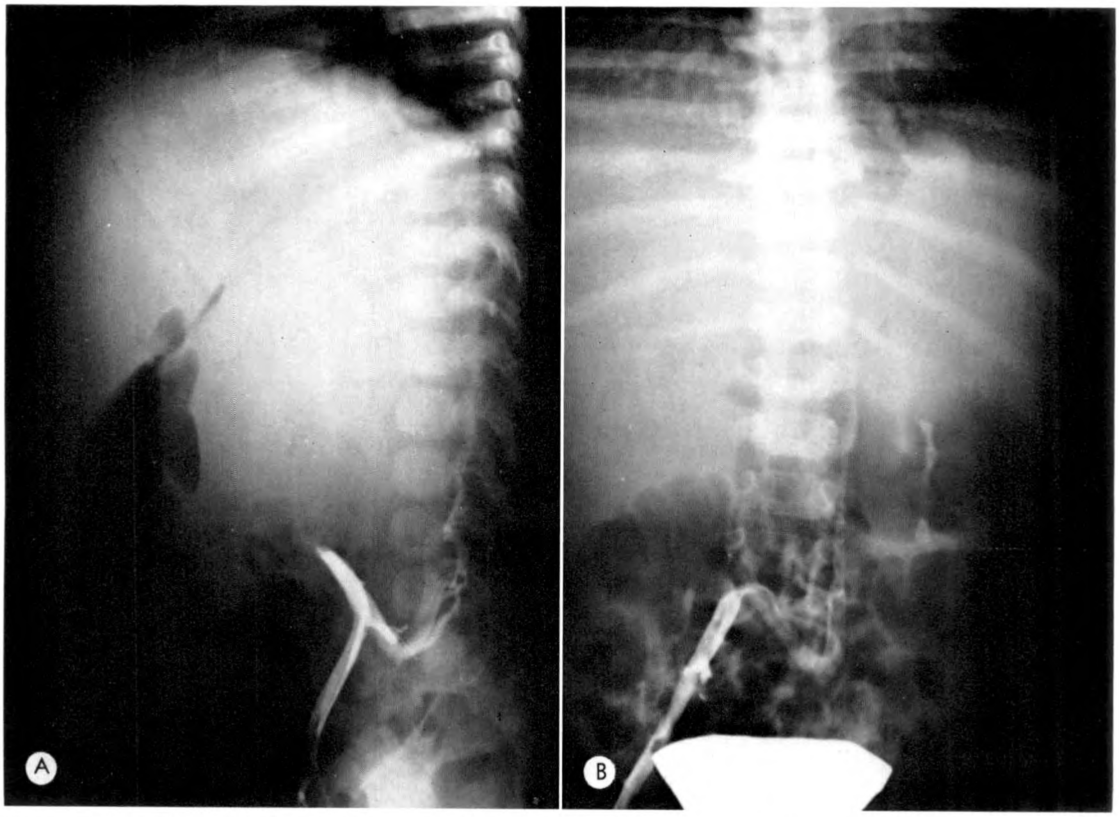

Fig. 9. (*A* and *B*) Inferior venacavagrams of this 13 month female were not very satisfactory because we were unable to inject a very large bolus into the child's saphenous vein. The right common iliac vein is displaced, accordion-like. The lateral view shows better filling of the lumbar veins than of the inferior vena cava, but the reverse is the case in the anteroposterior view. The latter shows a metastatic tumor nodule in the base of the left lung.

displaced the right-sided abdominal organs into the left side of the abdomen. It was readily resected and removed *in toto*. The right kidney and adrenal were normal, and were easily returned to their normal bed after removal of the tumor. The pathologic diagnosis of the specimen was cystic embryonal mesonephroma of adrenal origin.

Other authors, interested in injecting larger boluses of contrast medium and avoiding possible errors in interpretation of inferior venacavagrams, have advocated injecting both femoral veins at once.[3] We have not used this technique because of the additional effort and time it involves. That we perhaps should do so is suggested by our experience with a 2 year old child with a Wilms' tumor (Fig. 12, *A* and *B*). Our initial inferior venacavagram, filled from the left femoral vein, showed a large collateral lumbar circulation (Fig. 13 *A*), and we interpreted it to indicate inferior vena cava block by tumor. Accordingly, the child was given actinomycin D and preoperative irradiation to a tumor dose of 2,250 rads in 9 days. Under this therapy the tumor mass shrank perceptibly, and exploratory laparotomy was carried out. Before the operation, however, inferior venacavagraphy was performed from the right femoral vein, and this showed no indication of an obstruction (Fig. 13 *B*). It seems unlikely that the therapy would have dissolved a tumor thrombus within the inferior vena cava in the 9 day interval. We must conclude that we erred in interpreting inferior vena cava block in the first instance.

PITFALLS IN DIAGNOSIS

Hemihypertrophy of the limbs has been found sometimes to be associated with the presence of abdominal masses.[1] If a child has a larger arm and leg on one side of the body than the other, it is wise to be on the lookout for abnormalities elsewhere. We have had 2 patients with hemihypertrophy who had abdominal tumors, one a neuroblastoma, the other a Wilms' tumor. The disparity in size of the limbs is very obvious in the roentgenograms of the latter patient (Fig. 14, *A* and *B*). The child had been thoroughly studied in the newborn period, and an intravenous urogram was considered to show a "normally functioning upper urinary system. However, the kidneys appear a little larger than normal" (Fig. 15, *A* and *B*).

With that remark the opportunity for making the diagnosis passed. The child's health remained generally good for 19 months, after which time she was operated upon for repair of an umbilical hernia. At surgery retroperitoneal masses were felt. Postoperatively, intravenous urography was carried out, which showed such severe displacement of the collecting system of the left kidney that, had we not known the kidney originally was in normal position, we might have assumed it was congenitally ectopic (Fig. 16, *A* and *B*). Another operation was carried out, and the left kidney was found to contain a very large Wilms' tumor. It was removed, and the patient was given radiation therapy. Just after her third birthday the patient succumbed, not to the tumor in the abdomen (autopsy revealed no abnormal growth in the abdomen) but to extensive metastases throughout the chest.

Another child, aged 2½ years, was seen in

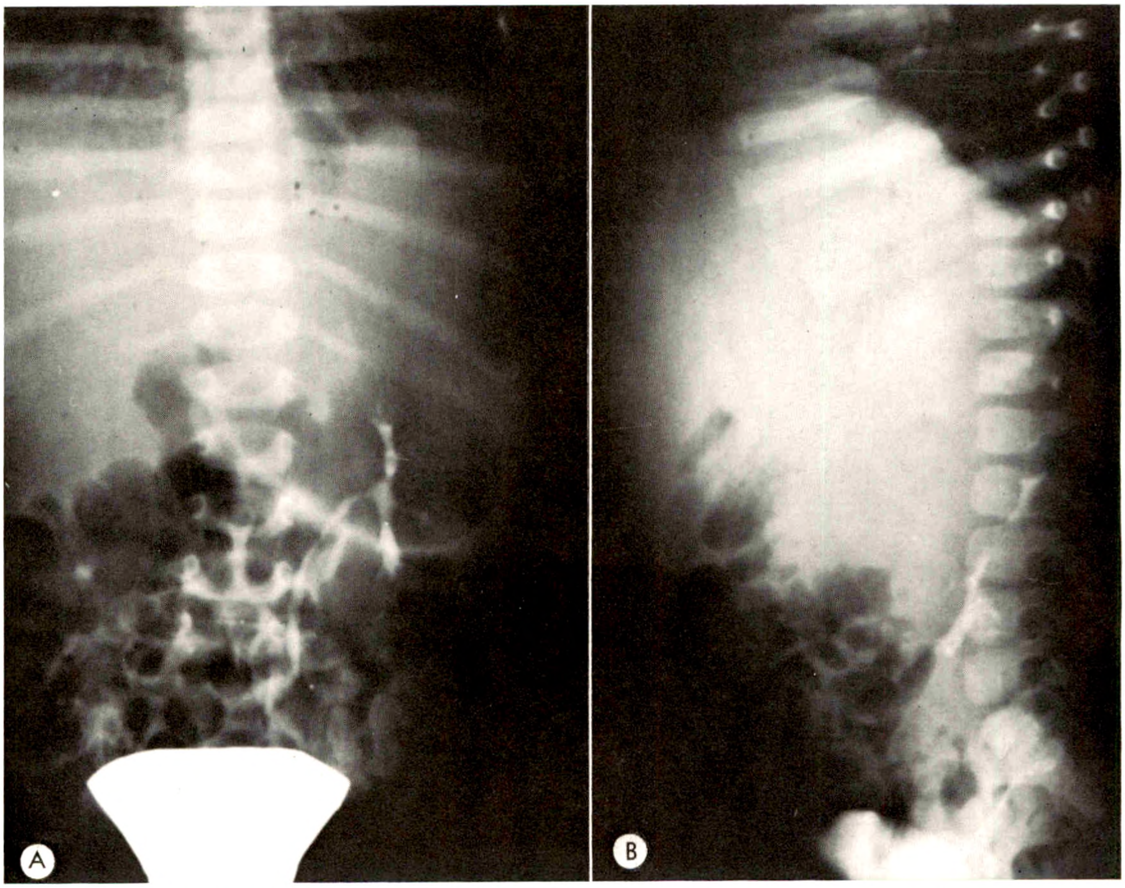

Fig. 10. (*A* and *B*) Anteroposterior and lateral roentgenograms made 10 minutes after the second inferior vena cava injection of the patient shown in Figure 9, *A* and *B* reveal a rather large left kidney and no excretory function on the right.

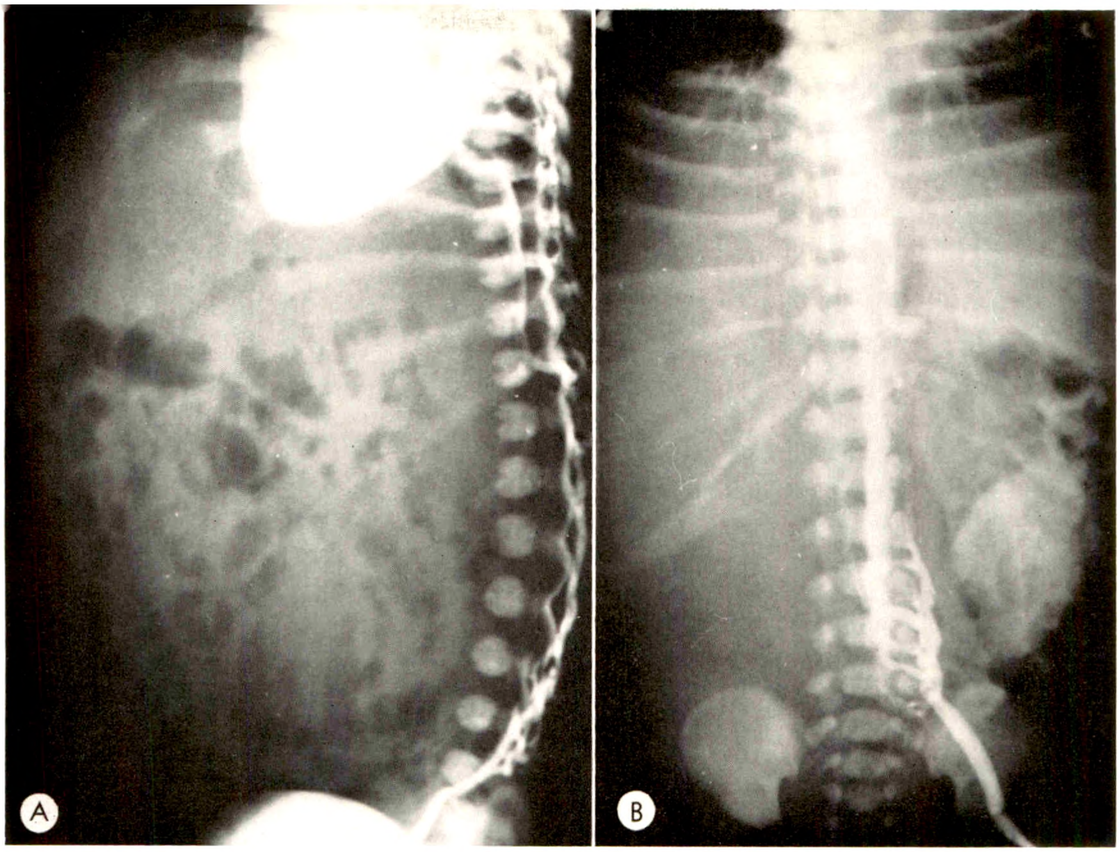

FIG. 11. (*A* and *B*) Inferior venacavagrams of a 2 day male with a huge right abdominal mass show no filling of the inferior vena cava but only the collateral circulation, which we atrributed to the tremendous size of the mass.

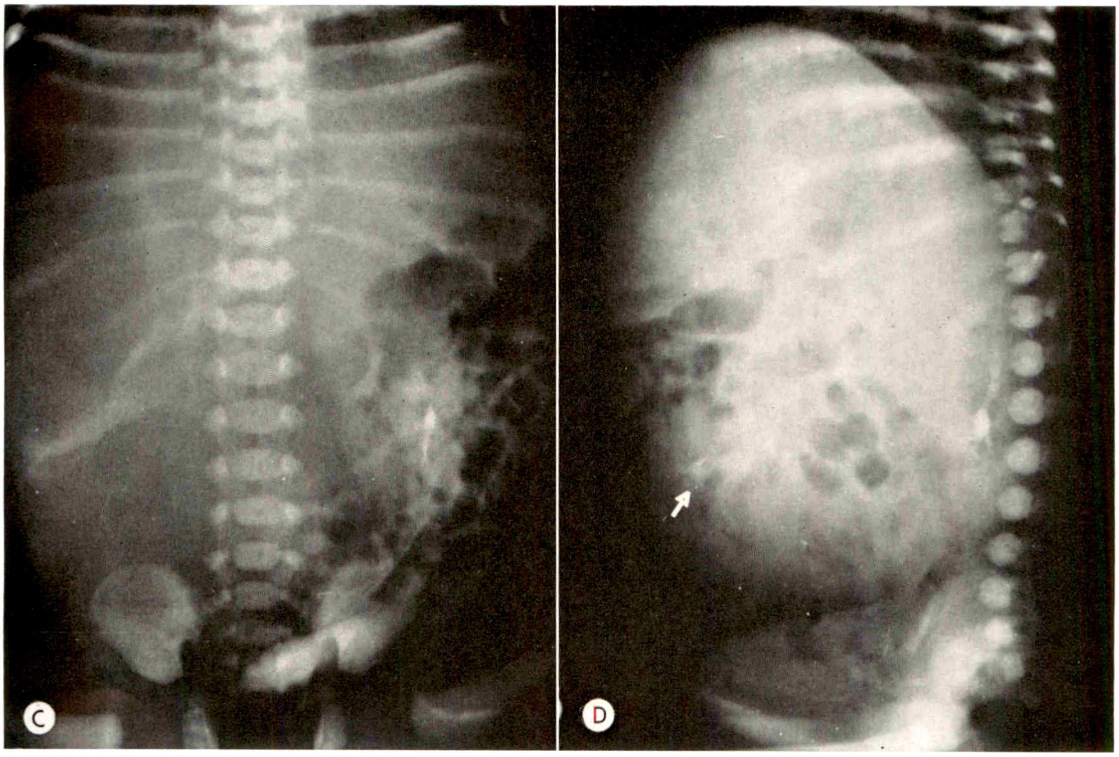

FIG. 11. (*C* and *D*) Follow-up roentgenograms show the right kidney displaced into the left side of the abdomen, projected on the anteroposterior roentgenogram to the left of the left kidney. In *D* an arrow points to the pelvis of the displaced right kidney. While the left side of the abdomen became denser following the intravenous injection, the right side remained unopacified except for a strand of tissue across its middle. This appearance was explained upon removal of the tumor, the mass being largely cystic but having vascularized septa which corresponded to the location of the strand in the roentgenograms.

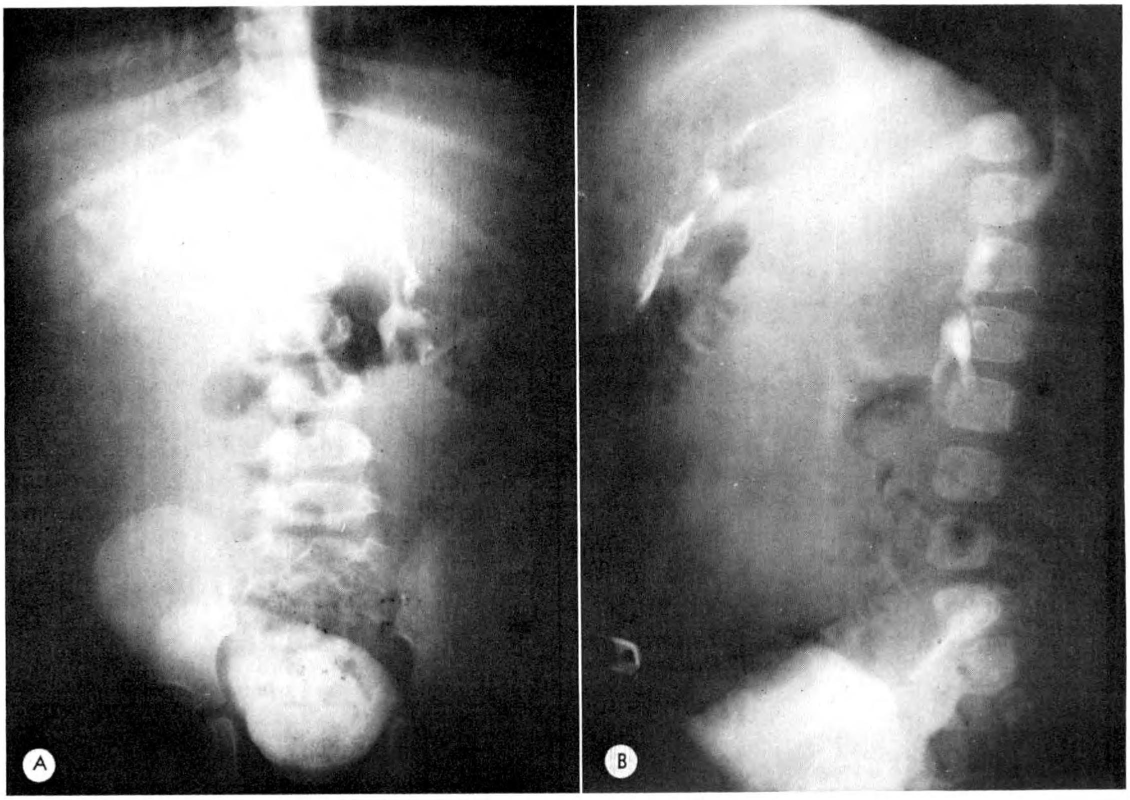

FIG. 12. (*A* and *B*) Intravenous urograms of a 2 year old child whose parents had noted abdominal swelling for 2 months but who otherwise had remained well.

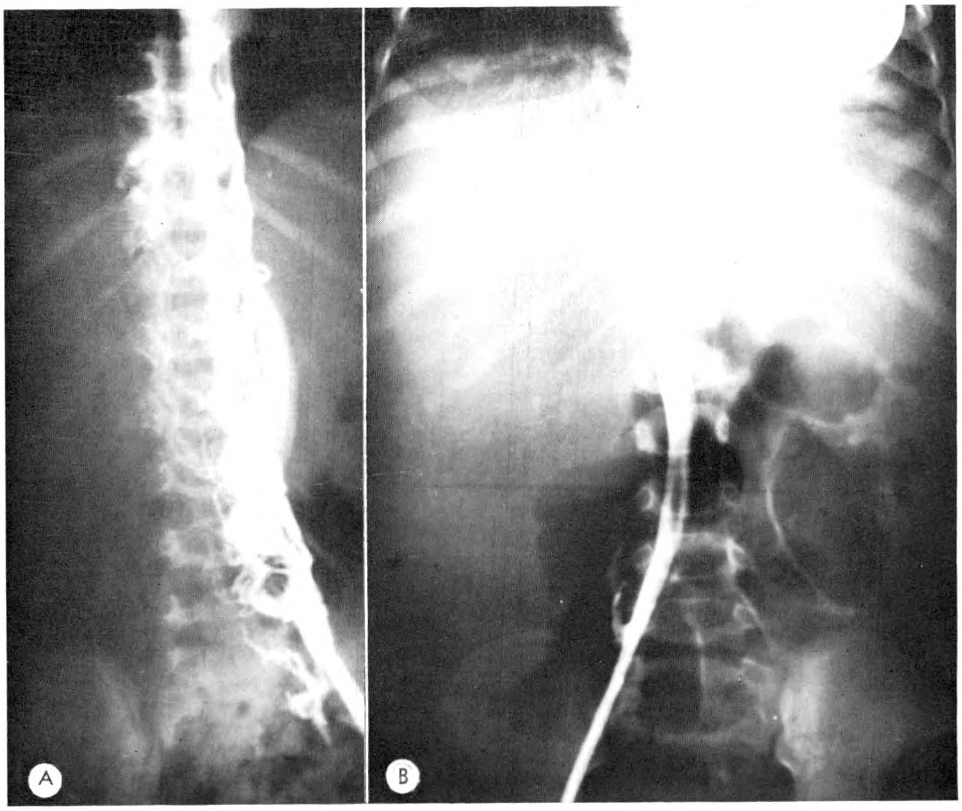

FIG. 13. (*A* and *B*) Inferior venacavagrams injected from (*A*) left femoral vein 2 days after the urograms in Figure 12, *A* and *B*, and (*B*) right femoral vein 11 days after the urograms. In *A* the patient is rotated slightly to the left. *B* shows better than Figure 12, *A* and *B* the faint but rather extensive calcification in the tumor of the right kidney. The kidney was removed. Histologic examination confirmed the impression of Wilms' tumor.

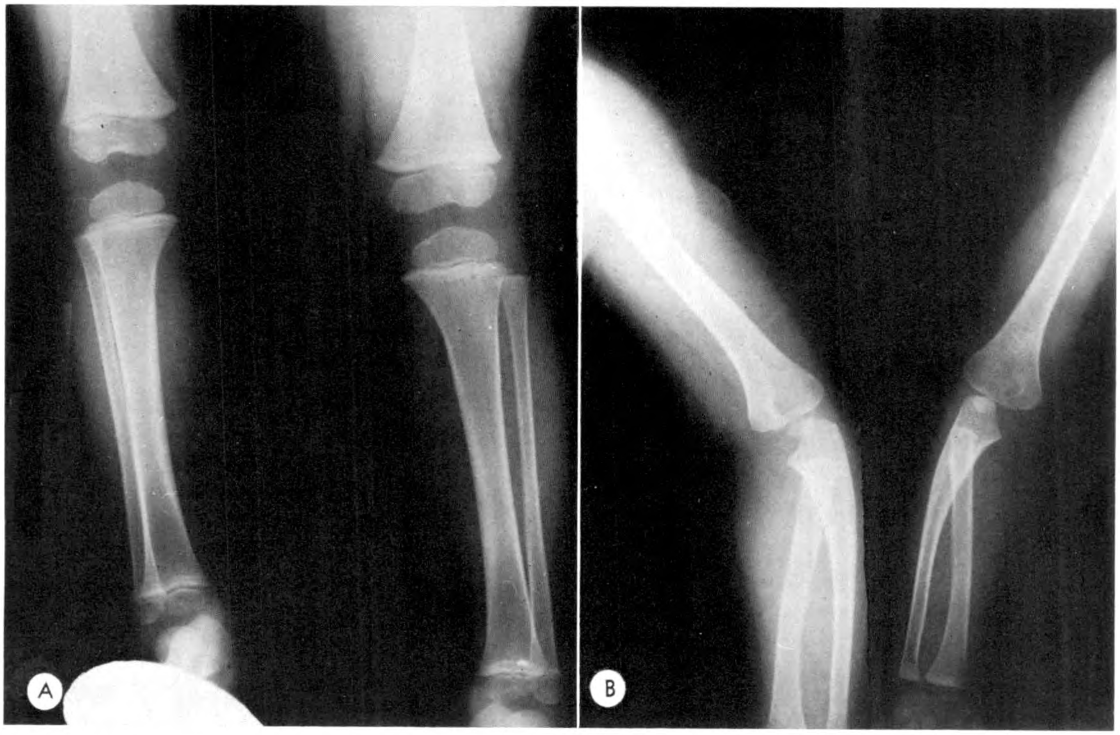

FIG. 14. (*A* and *B*) Anteroposterior roentgenograms of the limbs of 2 year old female whose left arm and leg are obviously much larger than her right.

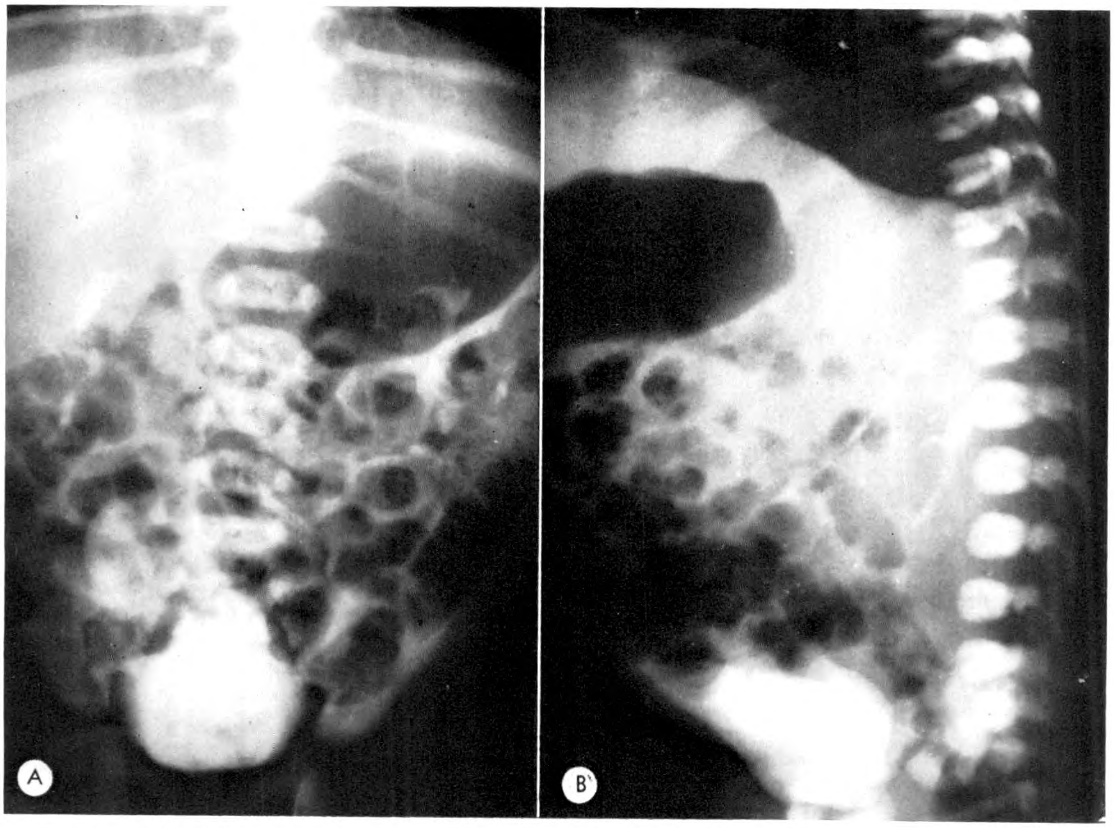

FIG. 15. (*A* and *B*) Intravenous urograms of the same patient shown in Figure 14, *A* and *B* in the newborn period.

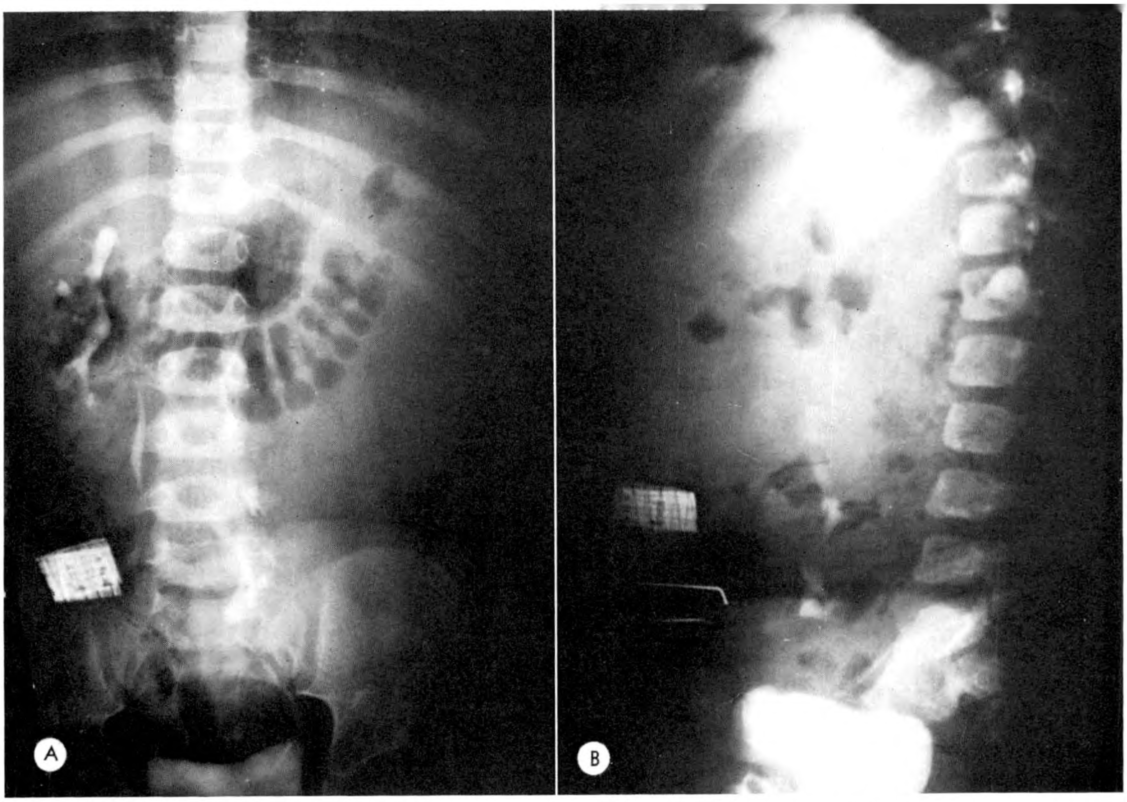

FIG. 16. (*A* and *B*) Same patient as shown in Figures 14, *A* and *B*; and 15, *A* and *B*. A huge left abdominal mass is present at 19 months, producing a displacement of the left kidney collecting system suggesting an extrinsic tumor. Operation, however, revealed the tumor to be a typical Wilms', with a preponderance of nephroblastic elements.

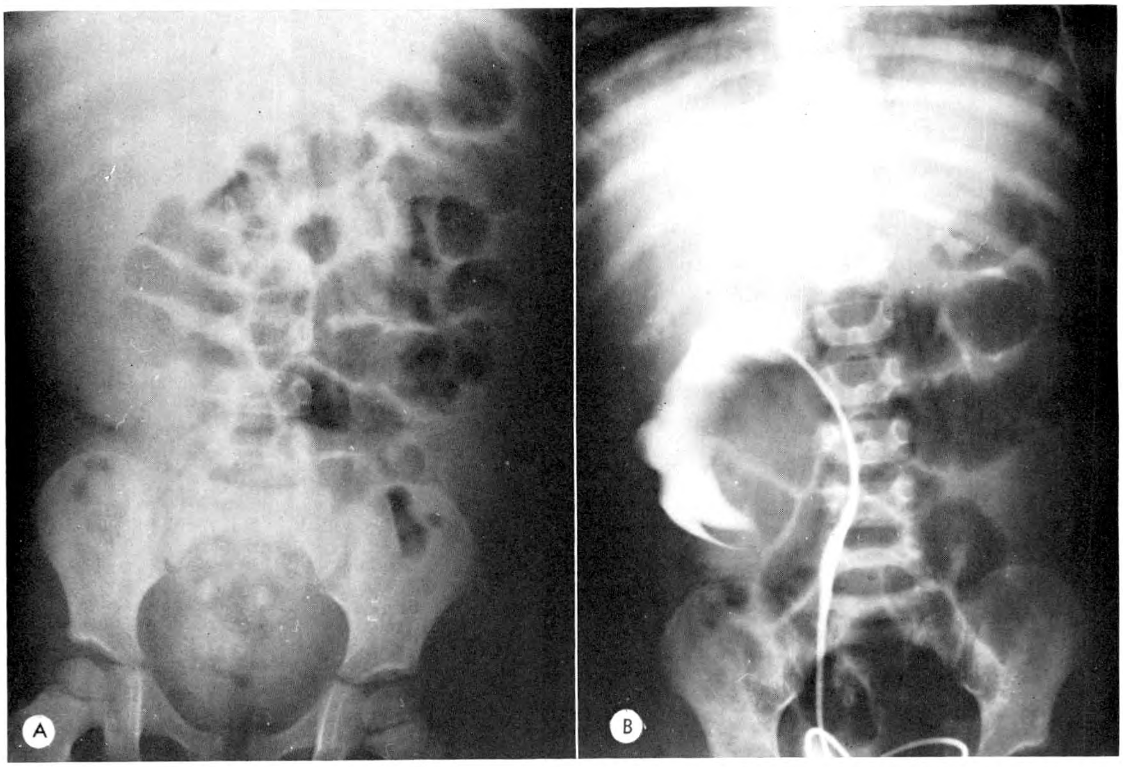

FIG. 17. (*A* and *B*) Roentgenograms made elsewhere of a 2½ year old female with a fever. The 3 minute urogram (*A*) shows excretion by the left kidney but not by the right, which is enlarged. A retrograde pyelogram (*B*), made immediately, showed the collecting system of the right kidney to be severely distorted by a tumor mass. Examination of the surgical specimen revealed it to be a Wilms' tumor. Although no pyelography was carried out on the left, the collecting system of the left kidney is readily visualized in *B* because of the prior intravenous urography, and a 2 cm. tumor is present in its mid-portion. (Roentgenograms by courtesy of Dr. R. A. Havill, Trumbull Memorial Hospital, Warren, Ohio.)

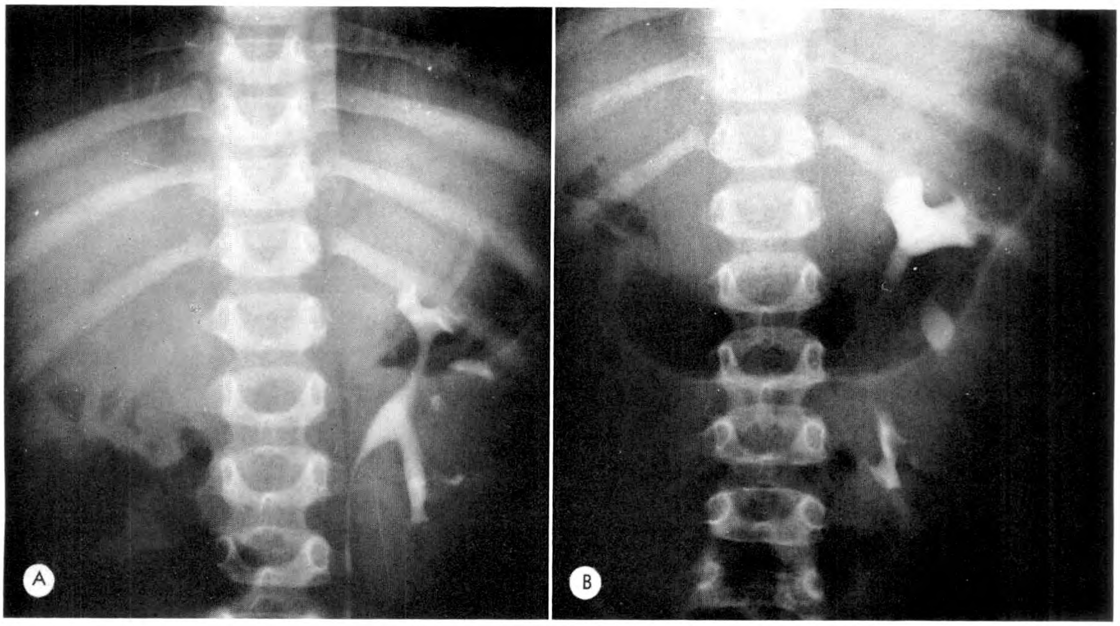

FIG. 18. Urograms made (*A*) 1 month and (*B*) 10 months after the studies in Figure 17, *A* and *B*. The tumor in the left kidney has increased manyfold in size.

another hospital because of fever. An intravenous urogram and retrograde pyelogram there showed a large tumor mass distorting the right kidney (Fig. 17, *A* and *B*), and it was removed. When the hyperpyrexia continued postoperatively, the patient was transferred to Babies and Childrens Hospital. On our urogram a mass lesion was found in the remaining kidney (Fig. 18 *A*), which had been present on the original study. One needs ever to be on constant lookout for more than one lesion in a patient. Radiologists should keep in mind that Wilms' tumors have been found to be bilateral in 3.6 per cent of reported cases,[12] and surgeons should be urged, whether the roentgenograms suggest a lesion in both kidneys or not, to explore both kidneys every time in order to avoid falling into this error.

We studied our patient with cineroentgenographic inferior venacavagraphy and right selective angiocardiography, and found tumor thrombus filling the inferior vena cava and bulging into the right atrium. In spite of actinomycin D treatment, the tumor in the left kidney continued to enlarge (Fig. 18 *B*), pulmonary metastases appeared, and the patient died 1 year after we first saw her.

CONCLUSION

Diatrizoate compounds are relatively safe and effective for intravenous injection in the evaluation of abdominal masses in children. The technique of inferior venacavagraphy is described, which provides information supplementary to that obtained by intravenous urography. It aids the management of tumors by furnishing information regarding resectability prior to surgery.

Pitfalls in interpretation of inferior venacavagrams and in management of tumors are discussed. Examples are given of two rare conditions, hemihypertrophy of the limbs and bilateral kidney involvement, which may occur with Wilms' tumors.

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THE DUCTUS BUMP*

A TRANSIENT PHYSIOLOGIC MASS IN CHEST ROENTGENOGRAMS OF NEWBORN INFANTS

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AN UNUSUAL appearing left mediastinal mass has been noted in chest roentgenograms of newborn infants. Though the patients presented sufficient clinical findings, usually of mild respiratory distress, to warrant roentgen study, *all* subsequently proved to be free of cardiac or pulmonary disease; the mass disappeared on serial roentgenograms. We believe the mass to be a reflection of neonatal adjustment to extrauterine life and to be the ductus arteriosus, patent and functioning, in the first 24 hours of life.

All patients noted to have the mass, herein termed the "ductus bump," were studied initially between 6 and 18 hours of life; all were full term, with a slight predilection for males. All infants had birth Apgar scores of over 5 indicating a lack of severe respiratory distress (10 would represent a lack of any complication; 1 or 2 would be a virtually dead infant).

The mass, seen to the left of the midline projecting from the mediastinum in frontal views (Fig. 1, 2, and 3*A*) could in no case be seen on lateral roentgenograms and did not indent the esophagus (Fig. 3*B*). It uniformly disappeared on serial frontal roentgenograms at 36, 48 and 72 hours of age.

The benign course, the subsequent absence of cardiac or pulmonary disease, the time of discovery of the mass plus its location and rapid disappearance led to the conclusion that the mass was *vascular* and that the changing hemodynamics of the first hours and days of life produced it and caused its regression. Only the ductus arteriosus is so located, so large at birth, and undergoes such rapid alteration in size, function, pressures and flow at this time of extrauterine life.

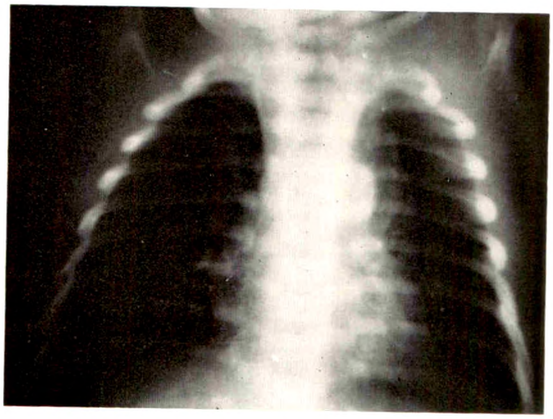

FIG. 1. A 3,200 gm. male infant with mild respiratory distress and pulmonic area systolic murmur heard at 18 hours of age. Note prominent ductus bulge that disappeared the next day.

HEMODYNAMIC ADAPTATION TO EXTRAUTERINE LIFE

In recent years, there have been many studies, both in animals[3,4,12,29] and humans,[1,4,6,7,10–13,8,20,22,23,26,28–32,36,37] detailing the cardiopulmonary status of the fetus and the changes required to permit extrauterine life. The work of Dawes[5,12] and his collaborators is outstanding.

The fetus lives in an environment designed to give maximum flow to the organ of fetal respiration and elimination, *i.e.*, the placenta. Oxygenated blood returns to the fetus from the placenta via the umbilical veins, mixing with fetal venous return. Right-to-left atrial shunts through the foramen ovale and right-to-left arterial

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† This study was completed while a scholar in Radiological Research of the James Picker Foundation.

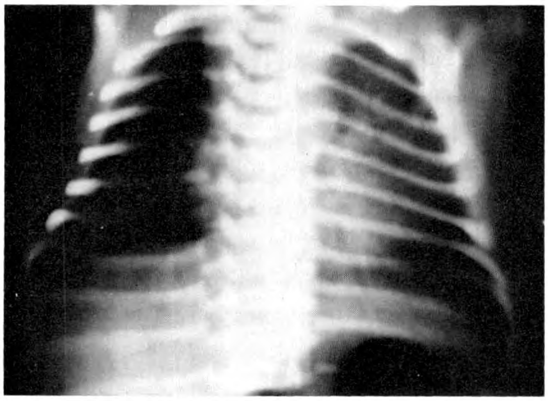

FIG. 2. A 2,900 gm. male infant with mild respiratory distress. At the age of 16 hours, a ductus bump density is seen in the left mediastinum.

shunts from the pulmonary artery through the ductus arteriosus to the aorta largely bypass the lungs and direct oxygenated blood to the fetal systemic circulation.

The lungs, though largely bypassed, do receive blood. Their small flow has been studied extensively. The intrapulmonary arteries and arterioles[11] have thick muscular walls and small lumens. This produces a *high* intrapulmonary vascular resistance; part of their small lumen diameter is produced by the contraction of fetal pulmonary arteries in the relatively low oxygen content of fetal pulmonary arterial flow.[12] The *high* resistance to such pulmonary flow preferentially shunts blood through the ductus to the aorta; the systemic arterial circulation is at a lower pressure than the pulmonary circuit. The blood that does go through the lung, circulating in the walls of the alveoli, bypasses the myriad small alveolar capillaries that will open with aeration of the lung.[28,29] The fetal pulmonary arterioles join pulmonary veins through virtually direct arteriovenous shunts. Thus, there are right-to-left intra- and extra-pulmonary shunts; these combine with the atrial right-to-left shunts to return oxygenated placental blood to the aorta, a *low* pressure system with *low* placental resistance.[5,12] With birth there must be a transition stage before the adult circulatory pattern is attained. Summarized, the adult circulation is a *high* pressure systemic circulation and *low* pressure pulmonary lesser circuit. The low resistance of the placenta is replaced by increased tone in the arterioles and capillaries of the systemic circulation. The atrial and ductal shunts having closed in the adult, the *high* pulmonary resistance has disappeared following birth. Pulmonary arterioles have lost their thick wall, small lumen character;[11,28,29] pulmonary capillaries of huge capacity bridge the arteriolar-venule level. The adult emerges as an organism with the organ of respiration (the lung) again a low pressure circuit with low resistance.

The infant in the first hours and days of life is in a middle world. Although deprived of placenta, the shunts that drained and

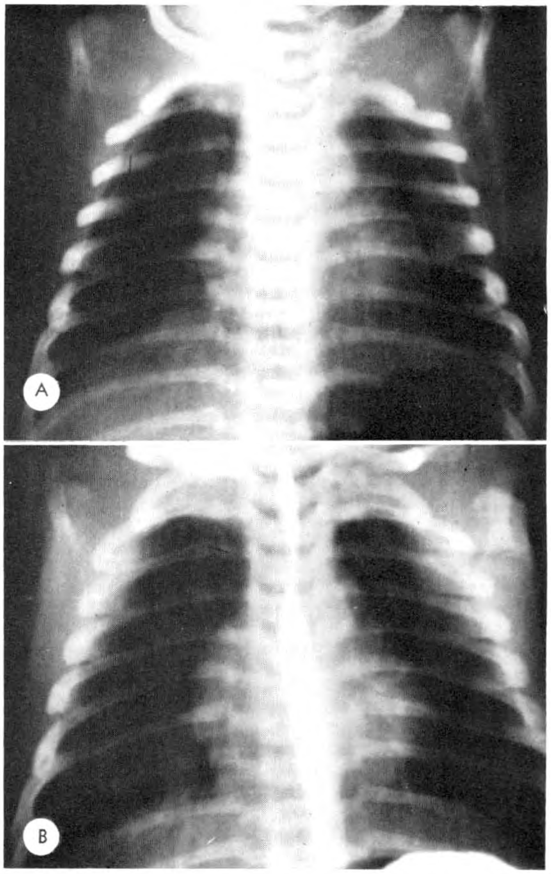

FIG. 3. A 3,100 gm. male infant with mild respiratory distress. (*A*) The mediastinal density is maximal at 18 hours of age. (*B*) Esophagram done at 2 days of age shows no indentation; the mass is virtually gone.

supplied that organ persist,[1,13,20,26,30,31,32,36] and although the lungs are expanded, the small arterioles retain high tone and resistance.

During this period of falling pulmonary pressures, ductal shunting continues; it may be right-to-left in the early hours. With each hour, aortic mean and diastolic pressures approach pulmonary levels. This leads to bidirectional and left-to-right shunting. Catheterization of infants during this first day of life,[1,13,30,31,32] as well as a smaller number of angiocardiographic cine-studies,[3,7,20] confirm the presence of ductal shunts of differing magnitude and direction. By the end of the first day, right-to-left ductal flow has virtually ceased but appreciable left-to-right flow continues. By 3 days the shunt is less and by 7 days virtually ended. Anatomic closure does not occur for several weeks.[4]

The ductus has the capability, even when deprived of nerve supply,[12] to contract in the presence of richly oxygenated blood and to dilate in anoxia;[36] large ductal shunts thus occur in anoxic states.[32,36] At this time, careful auscultation of the pulmonary area in normal infants reveals a majority to have a systolic murmur,[6] the "ductus flow murmur"; this is regarded as indicative of the patent ductus with still existent left-to-right flow. Thus, the ductus reacts in the opposite fashion to the intrapulmonary arteries; the latter *dilate* while the ductus *contracts* in rich oxygenated environment. Were this not to occur after birth, pulmonary hypertension, normal in the fetus, would persist.

Mean pulmonary artery pressures[13,30] are approximately equal or even higher than mean aortic pressures in the first hours of life; the pulmonary artery diastolic pressures are often higher than aortic diastolic levels even where mean values are equal. By day 2, aortic pressures are slowly rising and pulmonary pressures rapidly dropping; by day 3 right sided pressures are near adult levels, approximately one-quarter to one-third of fetal normals. Left sided systemic pressures take much longer to rise to adult levels.

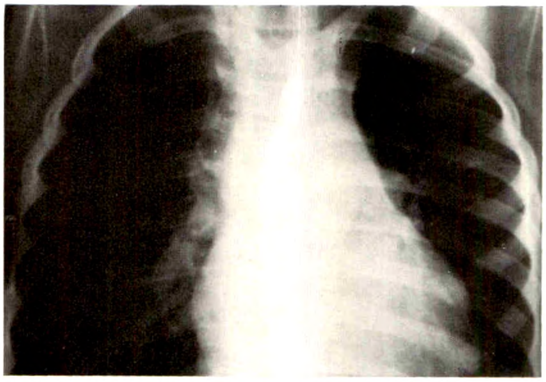

Fig. 4. In infancy a large ductus was ligated; at 8 years of age the ductal infundibulum persists, producing a mediastinal bulge below the aortic arch.

ANATOMIC CONSIDERATIONS OF THE DUCTUS ARTERIOSUS

The ductus arteriosus[4,37] is a large muscular tube connecting the pulmonary artery (near the origin of the left pulmonary artery) with the aorta, joining it on the ventrolateral aspect of the descending aorta. In the adult with a still patent ductus,[18] this ductus-aortic juncture may be seen on conventional chest roentgenograms; it then presents as a bulge of the mediastinum, mimicking a large aortic arch but is actually the ductus displacing the mediastinal pleura laterally just below the true arch. This may occasionally be seen in children even after ductal division (Fig. 4). The adult aortic arch and descending aorta project to the left of the mediastinum on frontal chest roentgenograms; senile "uncoiling of the aorta" accentuates this.

The infant aorta is not usually visible on frontal chest roentgenograms; its arch is hidden within the mediastinum.[7,8,10,20,24,27,34,35] The heart with the high right sided pressures shows right ventricular relative dilatation and prominence; thus the heart is rotated clockwise, and, in so doing, rotates the aorta medially. This explains the relative prominence at this time of the pulmonary artery segment and right ventricular outflow tract. The ductus, directed toward the ventrolateral aspect of the descending aorta, courses posteriorly and slightly *medially*. This is the opposite of its course in adults where it inserts laterally to the

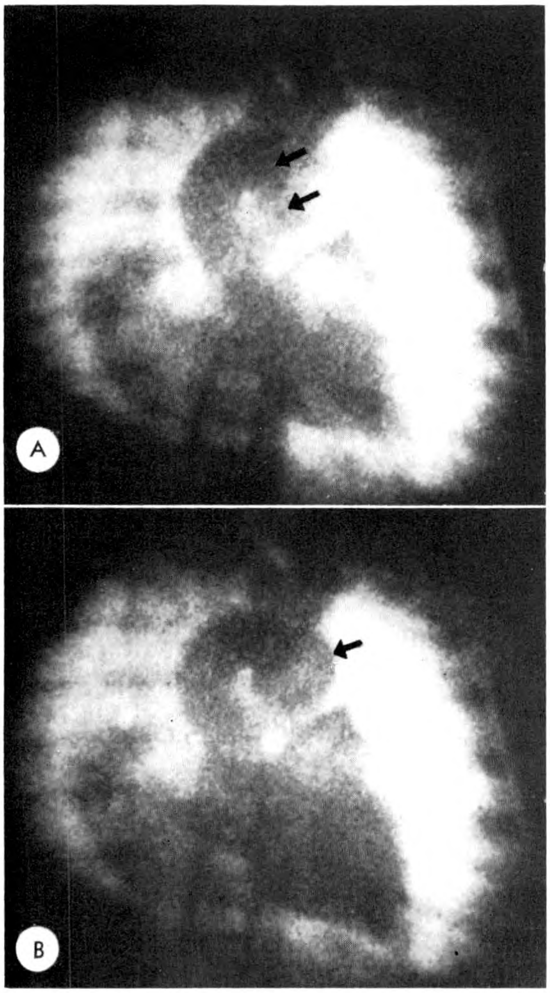

FIG. 5. (*A*) Left atrial injection via umbilical vein catheter in a noncardiac trisomy 21 newborn. The opacified aortic arch and descending aorta are medial to the ductus bulge. The arrows indicate the lateral aortic border. (*B*) Several frames later, the ductus, densely opacified, is seen. Cine-study shows diastolic dilution from the higher end diastolic pressures in the pulmonary artery. Systolic flow was left-to-right from the aorta. The arrow points to the patent ductus arteriosus.

mediastinum, producing the "infundibular sign" of the ductus noted by Jönsson and Saltzman.[18]

For these reasons, we believe that there is good basis for our interpretation of the mass seen in the first day of life as being the ductus arteriosus. It is also apparent that the main pulmonary artery forms virtually a straight line communication with the ductus and may contribute to the bump. With lowering of pulmonary vascular resistance and increased oxygenation, there are multiple forces set in play to dilate the pulmonary vessels and constrict the ductus; first the flow reverses, then it drops. This functional closure precedes by weeks anatomic closure; the latter normally follows ductal intimal roughening and final thrombosis.[4,37]

CINE-ANGIOCARDIOGRAPHIC STUDIES OF DUCTUS ARTERIOSUS

Observations of fetal and newborn cineangiocardiograms in animals and humans are in good agreement with the studies referred to.[3,7,20]

Contrast studies have been done both via the umbilical vein and umbilical artery. The vein gives access to the left atrium via the ductus venosus, right atrium and foramen ovale. The artery can direct contrast agent to the ductus with injection in the aorta at its aortic end, or even with the catheter in the ductus or pulmonary artery via the ductus.[3,7,13] Recent studies with such routes utilized in newborns[13] have unfortunately omitted roentgen examination, utilizing only catheterization data. Since our patients with the ductus bump have *not* had such cine-studies, we were able to correlate the plain roentgenographic findings with the cine-studies done on normal (though trisomy 21) newborn infants by Burnard and James.[7] When the injection is made in the left atrium, (Fig. 5, *A* and *B*) the aorta fills clearly, showing the medial location of the arch and descending portion. Adjacent to it is the ductal mass. The ductus fills during systole with aortic contrast agent; in diastole, higher pulmonary diastolic levels cause dilution. Burnard and James[7] noted the mass of the ductus to be denser than that of the aorta, indicating its greater depth. They observed the bidirectional flow and concluded that the mass was the ductus. Aortic injections on another infant (Fig. 6*A*) filled the mass readily, with the lateral view (Fig. 6*B*) showing the ductus and its direct continuation with the main pulmonary artery.

The case then for the ductus bump actually being the ductus is, at present, circumstantial. Until it is possible to perform cine- and catheterization studies on those patients with the bump in the first hours of life, it is likely to remain so.

THE DUCTUS BUMP IN AIRBLOCK OF THE NEWBORN (PNEUMOMEDIASTINUM)

Given impetus by the beautifully conceived studies of the Macklins[22,23] on interstitial emphysema-pneumomediastinum-pneumothorax as signs of "airblock," there have been many clinical studies relating this to pneumomediastinum in the newborn.[2,8,9,15,16,17,19,21,25,33]

Pneumomediastinum at birth, with or without pneumothorax, is generally benign in outcome and self-limited in course. Either aspiration with the development of endobronchial obstruction leads to ball-valve air trapping, rupture and leakage or uneven expansion of the lung at birth;[10] has shearing forces develop leading to alveolar rupture and air leak.

Such interstitial air leaks back along arterial and venous sheaths to the mediastinum where they accumulate as pneumomediastinum. If enough pressure develops, the air breaks through the mediastinal pleura, producing unilateral or bilateral pneumothorax (Fig. 7*A* and 8*A*).[22,23] The mediastinal air, though impressive on roentgenograms, rarely causes cardiac tamponade in the newborn infant and rarely leaks to the neck or below the diaphragm.[9] Presumably this reflects pressure levels of insufficient degree to produce generalized subcutaneous emphysema.

The mediastinal air, within this semi-closed space, forces the main pulmonary artery downward (Fig. 7, *B* and *C*) into a more direct course with the ductus. In addition, the intrapulmonary vessels are compressed by air in their vascular sheaths. It is, therefore, not surprising that the largest ductus bumps have been seen in airblock patients (Fig. 7, *A* and *B*).

Once again, catheterization and cinestudies are lacking; this reflects both the benign course of airblock patients, in general, and the only recent trend to such use of umbilical vessels. The lack of serious sequelae in most patients and their well being while showing dramatic pneumomediastinum on roentgen studies suggest that there are probably no serious alterations in pressure relationships between pulmonary and aortic circuits.

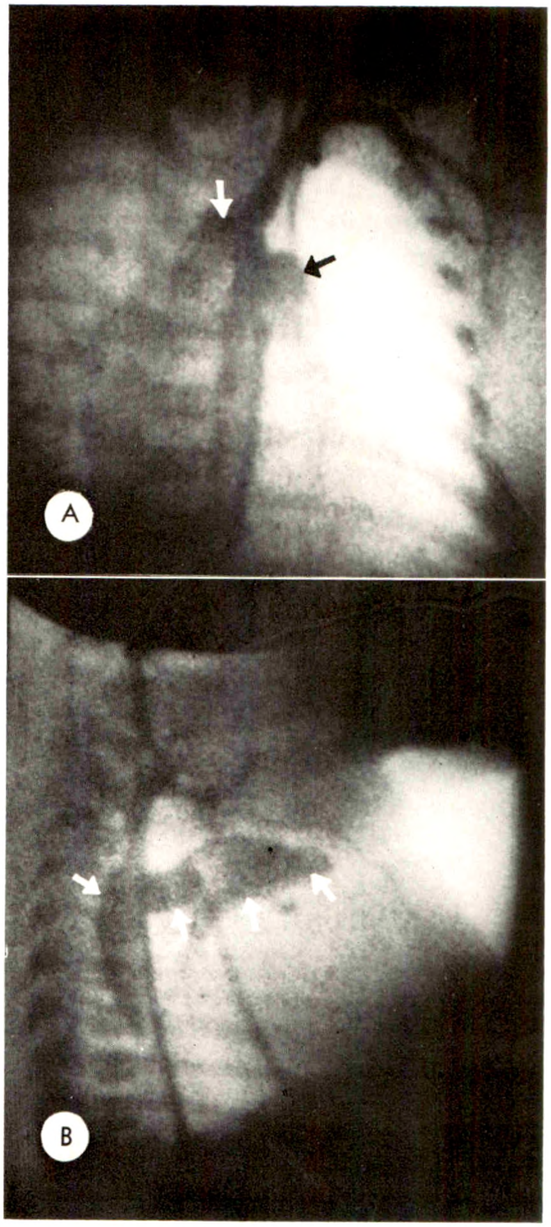

FIG. 6. (*A*) Frontal aortic injection via umbilical artery catheter shows ductal filling. Left arrow points to aorta, right arrow to patent ductus arteriosus. (*B*) Lateral study shows direct flow from aorta to ductus to main pulmonary artery. Note the almost straight line relation of the ductus and pulmonary artery. Left lateral arrow indicates the aorta, left central arrow the patent ductus arteriosus, right central arrow the main pulmonary artery, and right lateral arrow the pulmonary vein.

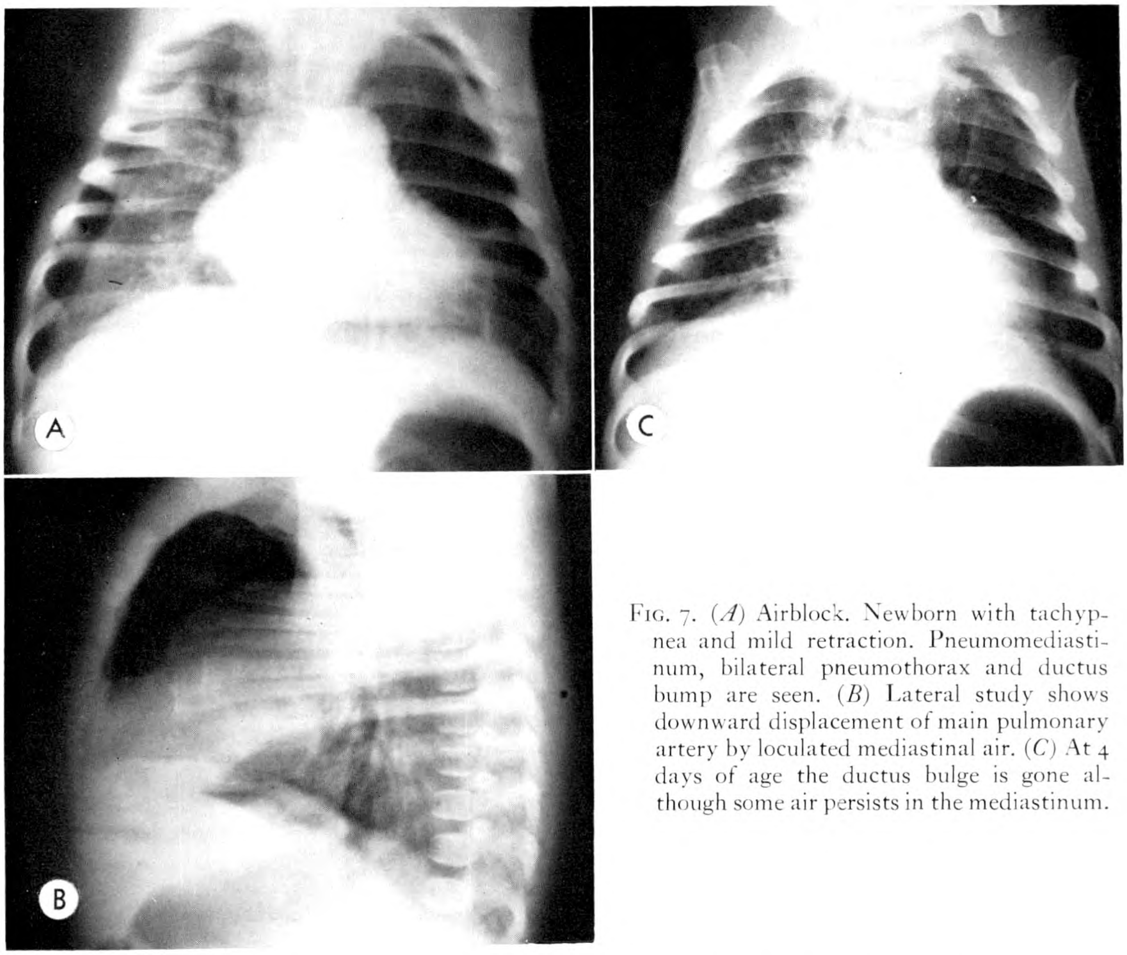

Fig. 7. (*A*) Airblock. Newborn with tachypnea and mild retraction. Pneumomediastinum, bilateral pneumothorax and ductus bump are seen. (*B*) Lateral study shows downward displacement of main pulmonary artery by loculated mediastinal air. (*C*) At 4 days of age the ductus bulge is gone although some air persists in the mediastinum.

CAN THE DUCTUS BUMP BE CONSIDERED NORMAL?

Our patients all are alive and well without any cardiac or pulmonary disease. This fact, plus the studies referred to, leads us to conclude that we are viewing a physiologic, *i.e.*, a nonpathologic, mass; in this regard, it is "normal." Yet, surveys of large numbers of chest roentgenograms in normal newborn infants,[7,10,14,20,24,27,34,35] as well as detailed pediatric chest roentgen interpretations,[8] fail to include the ductus bump; usually studies have centered on content of aeration and pulmonary densities. Little attention has been related to cardiac findings and pulmonary vascular changes.[7] The role of the thymus in making up the newborn mediastinal "cardiothymic image" has been strongly challenged[7] by those who feel that the heart is the predominant part at this age.

We would add the ductus bump to the range of normal at the age of birth to 1 to 2 days. Its role in "airblock" findings could also be regarded as "normal," reflecting mechanical changes in orientation of the pulmonary artery and ductus.

Unexplained by these observations is the *rarity* of the ductus bump. Although 15 good cases and a larger number of questionable examples have been found in 2 years of study, this constitutes a very small percentage of the total number of chest roentgenograms seen in the newborn. It has been noted that the vast majority of chest roentgenograms of newborn infants at Babies Hospital are of premature infants, contrasted with the full term status of ductus bump cases. Perhaps this lack of ductus bumps in premature cases with respiratory distress relates to *in utero* premature ductus contraction;[4,37] such contraction has been observed much more commonly in postmortem examinations of premature infants dying of respiratory distress than in com-

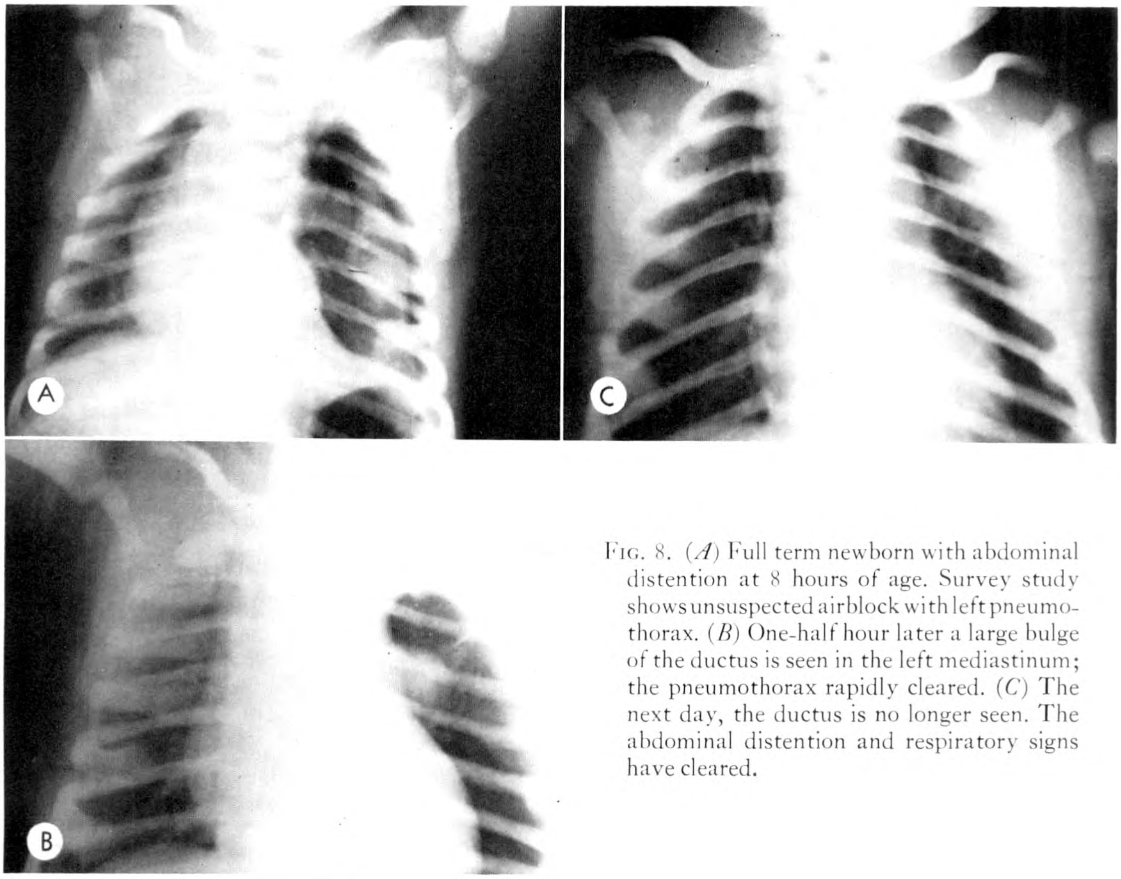

Fig. 8. (*A*) Full term newborn with abdominal distention at 8 hours of age. Survey study shows unsuspected airblock with left pneumothorax. (*B*) One-half hour later a large bulge of the ductus is seen in the left mediastinum; the pneumothorax rapidly cleared. (*C*) The next day, the ductus is no longer seen. The abdominal distention and respiratory signs have cleared.

parably studied full term infants.

Finally, chest roentgenograms taken later than the first day of life will have the disadvantage of having missed the period when the pressures and shunts would reveal the ductus bump.

SUMMARY

The ductus arteriosus may appear as a left mediastinal mass, the "ductus bump," on chest roentgenograms of the newborn infant. "Airblock" (pneumomediastinum) accentuates the findings. The current knowledge of the first day of life hemodynamic adjustments is reviewed, including catheterization and cine-angiographic studies. These lead to the conclusion that the ductus bump is a "normal" mass, transient and physiologic, presenting on chest roentgenogram of infants in the first day of life.

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CONTROLLED PULMONARY ROENTGENOGRAPHIC EXPOSURES IN NEWBORN INFANTS*

By A. EDWARD O'HARA, M.D.,† JOHN D. WALLACE, A.B.,‡ *and* R. E. NERLINGER§
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GADGETRY is the handmaiden of the radiologist and as a result we all have to keep an active interest in this field. At times, our work can be made easier or its quality improved by the addition of a new piece of equipment or circuitry.

Numerous mistakes in proper interpretation of chest roentgenograms of infants are directly due to faulty inspiratory techniques. In an attempt to obtain consistent roentgenograms in full or nearly full inspiration, one will see the pediatric technician tightly clutching the exposure button and going through all kinds of motion keeping time with the infant's or child's breathing. Finally, after some time of doing her "specialty dance," the exposure is made and, frequently, on viewing the final roentgenogram we find that it is in a poor phase of inspiration. This may be true of the expert as well as the technician with little experience in pediatric techniques.

In the Air-Shields Infant Isolette Respirator, a sensor is used to control the assist component of the respirator. We are indebted to Dr. H. S. Harned, Jr.,[1] of North Carolina Medical Center for the idea of using this same mechanism to trigger the roentgen-ray exposure of the chest at peak inspiration.

EQUIPMENT

The Air-Shields Actuator utilizes a small molded plastic nose mask (Fig. 1) in which is mounted a crystal thermistor sensor.[2,3] The sensor is located in the mask in such a way that the dead space is reduced to a minimum. The mask is placed over the infant's nose and taped in place (Fig. 2 and 3). The air that is inspired is relatively cool and passes over the thermistor on its way to the lungs. In doing so, the thermistor's resistance is increased. Warm air expired from the tracheobronchial tree reduces the resistance in the termistor. The slight change in temperature registered by the thermistor as respiration changes from inspiration to expiration can thus be utilized to trigger the roentgen-ray exposure. The unit has been so designed that the amplified signals from the thermistor are monitored by the control box (Fig. 4). When the technician desires to make the exposure, she merely presses the exposure button on the control box and a roentgenogram is obtained in the next peak inspiration. The monitor reset button has to be pressed before a second exposure can be made, thus preventing repeated exposures. The unit will actuate the roentgen-ray exposure 0.05 seconds following the peak of inspira-

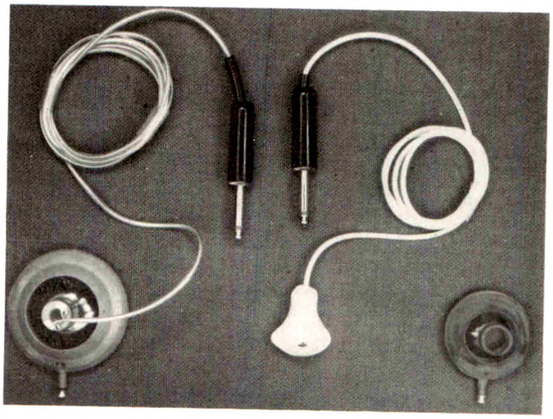

Fig. 1. The plastic molded nose mask (center), used in roentgenography on all newborns and infants, is illustrated above. Note the location of the crystal thermistor and connecting wire for the monitoring box. The small infant anesthetic masks have been adapted for older infants and children.

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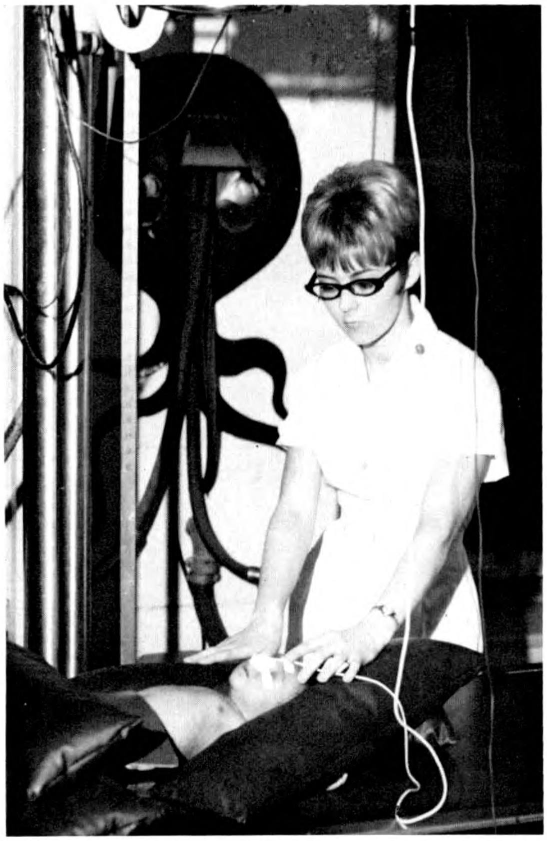

FIG. 2. The method of positioning the infant for the chest examination and the placement of the nose mask are illustrated at left. Note the wires for connection to the monitoring box.

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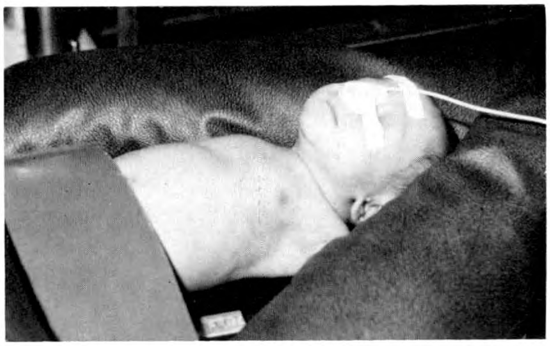
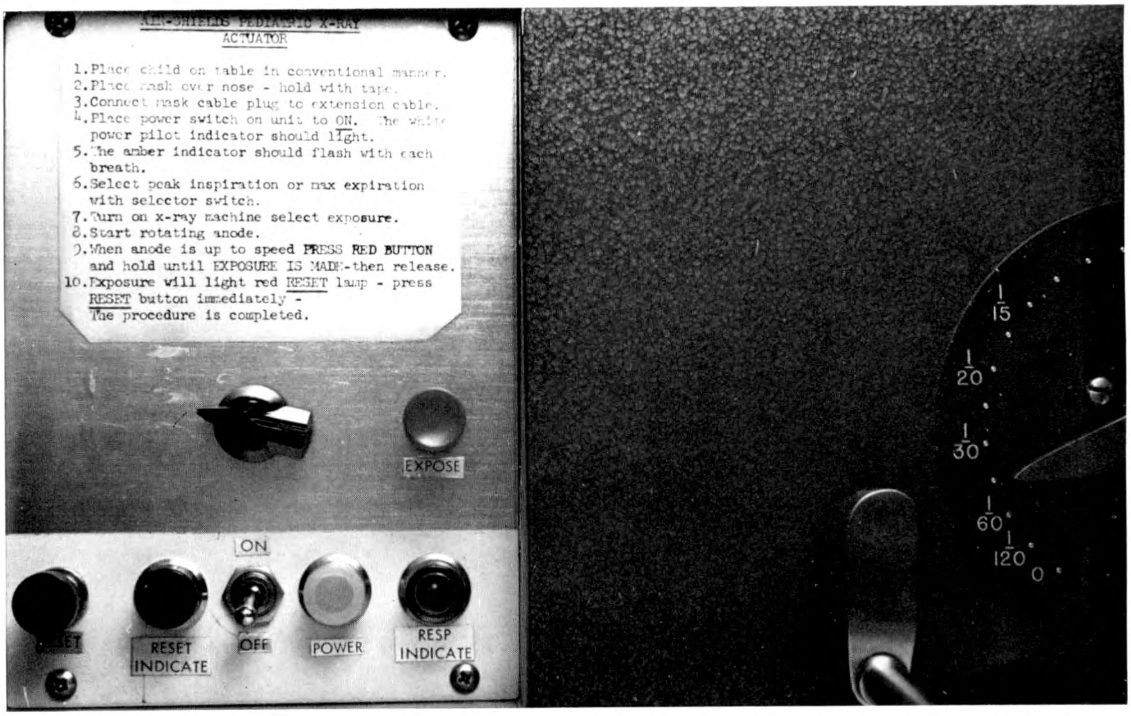


FIG. 3. Placement of the nose mask is illustrated above.



AIR-SHIELDS PEDIATRIC X-RAY
ACTUATOR

1. Place child on table in conventional manner.
2. Place mask over nose - hold with tape.
3. Connect mask cable plug to extension cable.
4. Place power switch on unit to ON. The white power pilot indicator should light.
5. The amber indicator should flash with each breath.
6. Select peak inspiration or max expiration with selector switch.
7. Turn on x-ray machine select exposure.
8. Start rotating anode.
9. When anode is up to speed PRESS RED BUTTON and hold until EXPOSURE IS MADE-then release.
10. Exposure will light red RESET lamp - press RESET button immediately - The procedure is completed.

FIG. 4. The monitoring box is illustrated above. Note the main switch, indicator light of infant's respiration, the exposure button and the reset button.

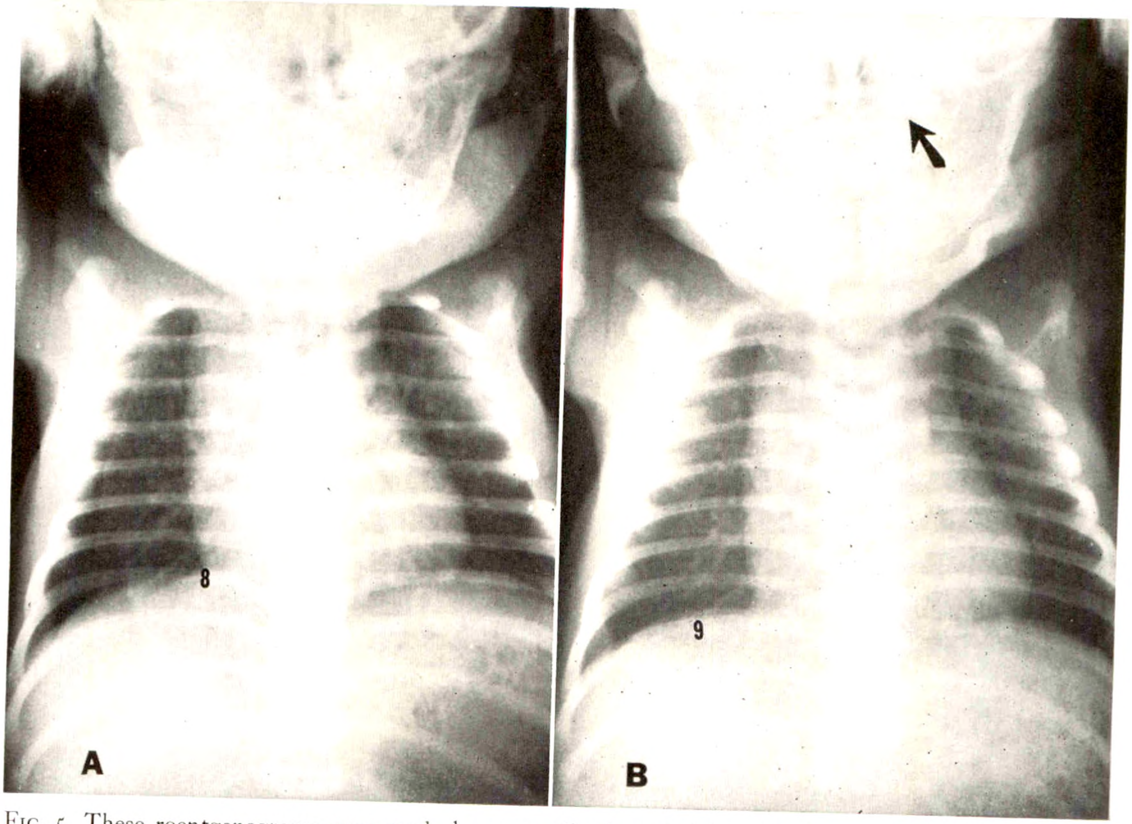


FIG. 5. These roentgenograms were made by our pediatric technician. (*A*) Roentgenogram manually exposed by the technician and (*B*) roentgenogram exposed by the monitoring device. Note the wiring mechanism within the nose mask (arrow).

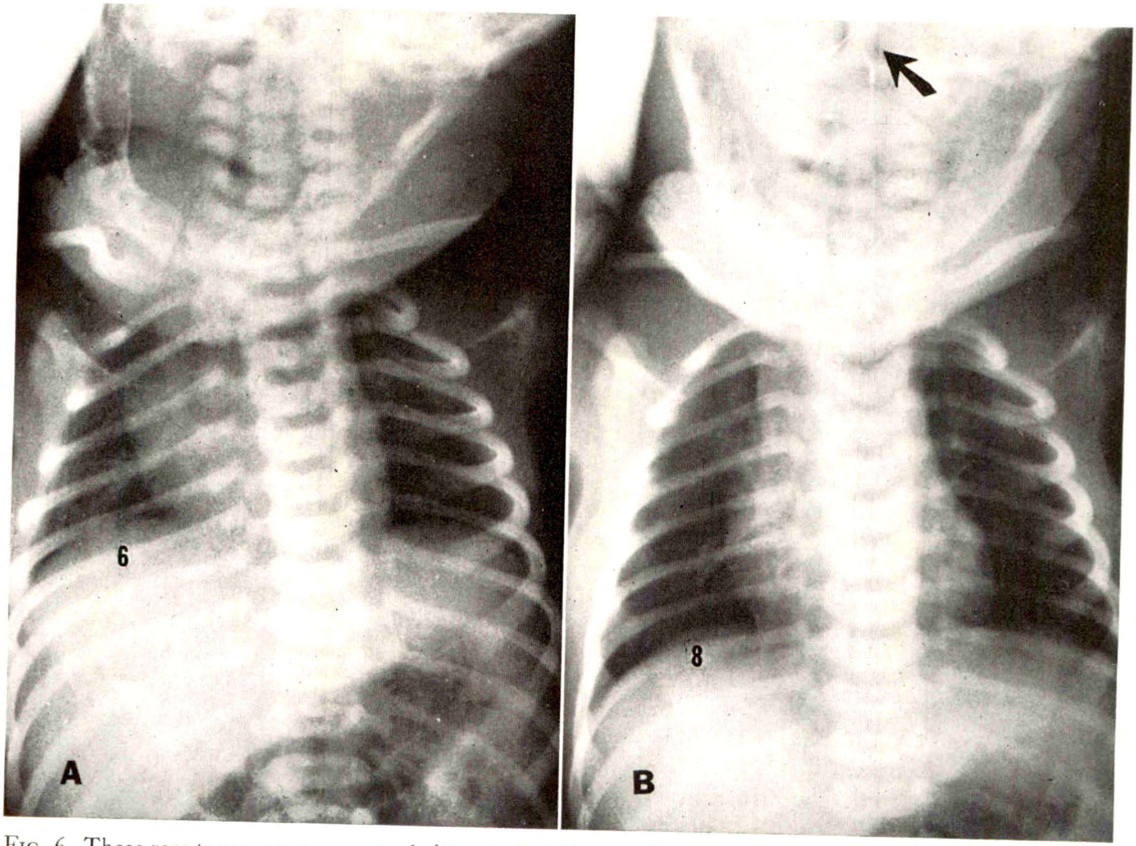


FIG. 6. These roentgenograms were made by a student technician. (*A*) Roentgenogram manually exposed by the student technician and (*B*) roentgenogram exposed by the monitoring device.

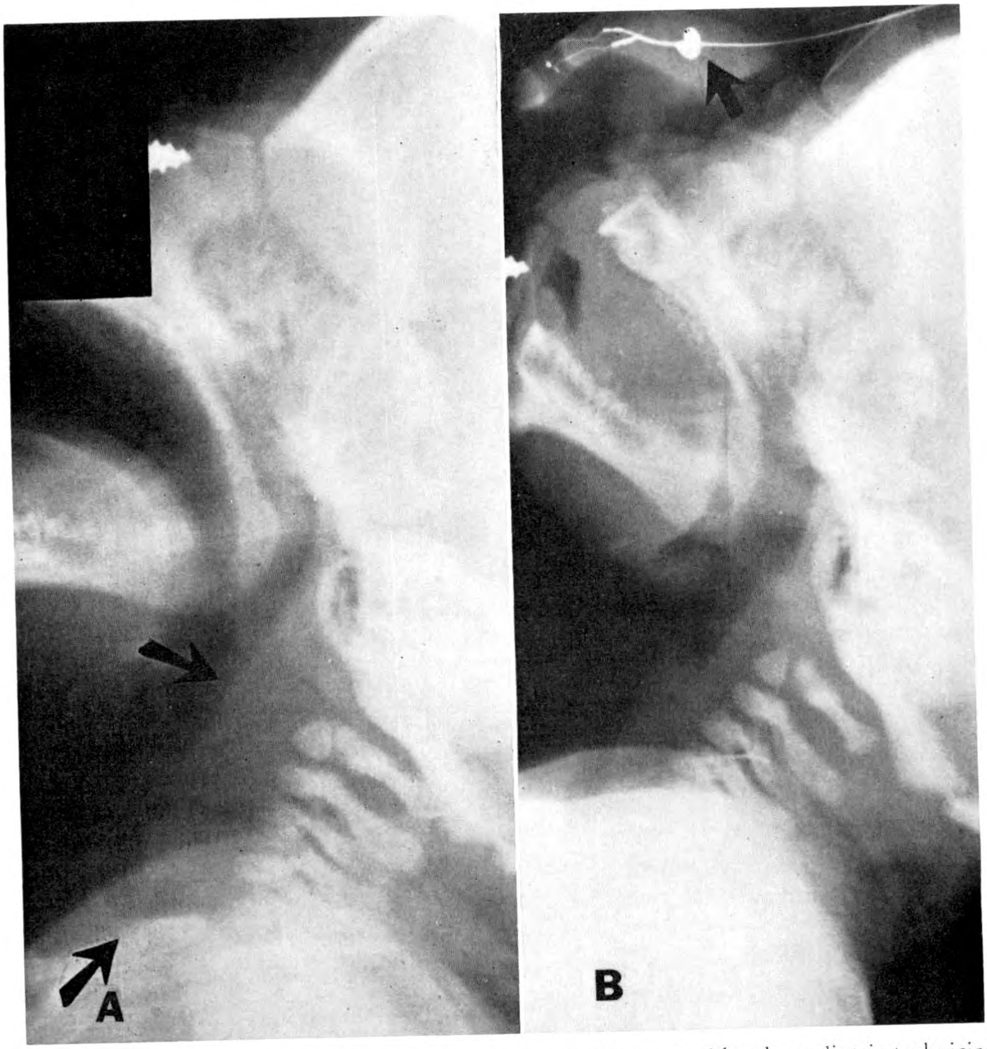


Fig. 7. (*A*) In this normal newborn, the roentgenogram manually exposed by the pediatric technician shows an apparent widening of the retropharyngeal soft tissues, simulating a mass or abscess (upper arrow). Because of the posterior buckling of the trachea (lower arrow), we realize this was made in expiration or poor inspiration. (*B*) This roentgenogram made on the same infant using the monitoring device (arrow) showed good inspiration, a straight trachea, and normal retropharyngeal soft tissues.

tion. The nose cone can be easily cleansed and sterilized with aqueous zepharin between cases. Before experimenting with roentgenography of infants, the unit was tested and correlated with their breathing patterns by means of respirograms. The signal was found to be consistent with the peak of inspiration.

CLINICAL MATERIAL

Subsequent to the confirming respirograms, over 100 infants from our newborn nursery were studied. Two anteroposterior exposures were made on each infant (Fig. 5, *A* and *B*), one by our pediatric technician and the second exposure by the monitoring device. In a subsequent group of 50 patients, a student technician compared her ability to obtain full inspiratory chest roentgenograms with that of the monitoring device (Fig. 6, *A* and *B*).

RESULTS

We have found that the monitoring device has been capable of consistently yielding roentgenograms made in close to full inspiration. On comparing these roentgenograms with those made by our pediatric technician, we found that she could match the degree of inspiration consistently, but she spent much longer time in obtaining good inspiratory roentgenograms. In the second group of patients, the roentgenograms obtained by utilizing the monitoring device were consistently superior to those obtained by the student technician.

We feel that this device can be adapted to use in older children and possibly adults by changing the size of the face mask. The possibility of using the same unit for triggering exposures in expiration has been suggested. This could be of great advantage in obtaining roentgenograms in timed expiration. The latter can be of vital importance in the study and documentation of aspirated foreign bodies, as well as bronchial and bronchiolar obstructions of other causes. Such a project is now under investigation.

In the study of the infant's retropharyngeal soft tissues, roentgenograms can be obtained in all phases of respiration. Those made in expiration or poor inspiration reveal a posterior buckling of the trachea and a widening of the retropharyngeal soft tissues, giving a false impression of a retropharyngeal mass or abscess. Because of the success we achieved in the anteroposterior views of the chest, we extended our investigation to the study of the lateral views of the neck, using the same method of investigation (Fig. 7, *A* and *B*). Here, as in the chest study, we found the monitoring device to be highly effective in ensuring a roentgenogram in good inspiration.

SUMMARY

We have described the Air-Shields Actuator and how it has been applied toward obtaining good inspiratory roentgenograms of the chest and lateral neck in newborns and infants. It is our feeling that this is a very reliable and timesaving device in pediatric radiologic practice. The ease of use and consistent results have readily made this a device which is quickly accepted by technicians and residents.

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PNEUMATOCELE FORMATION COMPLICATING HYDROCARBON PNEUMONITIS*

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INGESTION of petroleum distillates accounts for 21 to 25 per cent of all fatal poisonings in children under the age of 5 years.[1,16] Between 1951 and 1958, 763 deaths in the United States were attributed to hydrocarbon ingestion. Ninety per cent of these were in children under 5 years of age.[22]

Complications resulting from the ingestion of petroleum distillates include central nervous system depression, degenerative and hemorrhagic changes in various viscera and pneumonitis.[14] Pneumonia and pulmonary edema are the greatest threat to life[22] and are of chief interest to the radiologist.

Many reports of hydrocarbon ingestion complicated by pneumonitis are found in the literature. [4,5,8,9,10,12,13,14,15,18,20,21,22,27,28] In 1948, Bolobna and Woody[4] reported a series of 252 cases of kerosene poisoning. Eighty per cent showed pulmonary abnormalities. Heacock,[15] in 1949, reported a series of 103 children, 60 of whom showed roentgenographic evidence of bronchopneumonia following hydrocarbon ingestion. Other large series include those of Foley *et al.*[9] in 1954 with 101 children, 50 of whom developed bronchopneumonia, and of McNally[20] in 1956 who reported 204 cases with a 30 per cent incidence of pulmonary infiltrations. In 1958, Bonte and Reynolds[5] reported a series of 65 patients and described and reviewed the roentgenographic changes. Sixty of their patients developed pneumonic infiltrations.

The largest recent series is found in the Report of the American Academy of Pediatrics Subcommittee on Accidental Poisoning. A cooperative kerosene poisoning study was carried out with 46 participating hospitals in the United States and Canada.[22] The number of patients studied was 767. Pneumonitis was the usual specific complication, occurring in 235 patients (38 per cent).

Only one instance of formation of cysts or pneumatoceles in hydrocarbon pneumonia has been reported in the English literature.[26]

Since 1959, we have observed 3 patients who developed pneumatoceles following the ingestion of petroleum distillates with ultimate progression to complete recovery.

REPORT OF CASES

CASE I. A 14 month old Negro female drank an unknown amount of "Kan-Kill"* 30 minutes prior to arrival in the emergency room. She had been discovered by her mother coughing, gasping and in obvious distress. Upon arrival in the emergency room, she vomited. Gastric lavage was done.

On physical examination, her temperature was 39.7°C., her pulse was 180 per minute and her respirations were 60 per minute.

The laboratory data included a white blood cell count of 11,800 with 38 per cent neutrophils and 40 per cent juvenile forms. Admission nasopharyngeal cultures grew "normal flora" and the throat culture yielded *E. coli*. The blood culture was negative.

A chest roentgenogram obtained the following day revealed extensive confluent bilateral basilar infiltrations and peripheral hyperaeration (Fig. 1*A*). The infiltration progressed becoming more confluent and dense 3 days later. During this interval, her course was stormy with continued respiratory symptoms and a temperature ranging between 38°C. and 39.5°C. A second throat culture grew pneumococci.

She was started on antibiotic and steroid therapy and became afebrile within the next 5

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* Petroleum distillates 97.708%, Chlordane 2.0%, N-Octyl bicyclocheptene dicarboximide 0.154%, Piperonyl butoxide 0.092% and Pyrethrins 0.046%.

* From the Department of Radiology, The Johns Hopkins University and Hospital, Baltimore, Maryland.

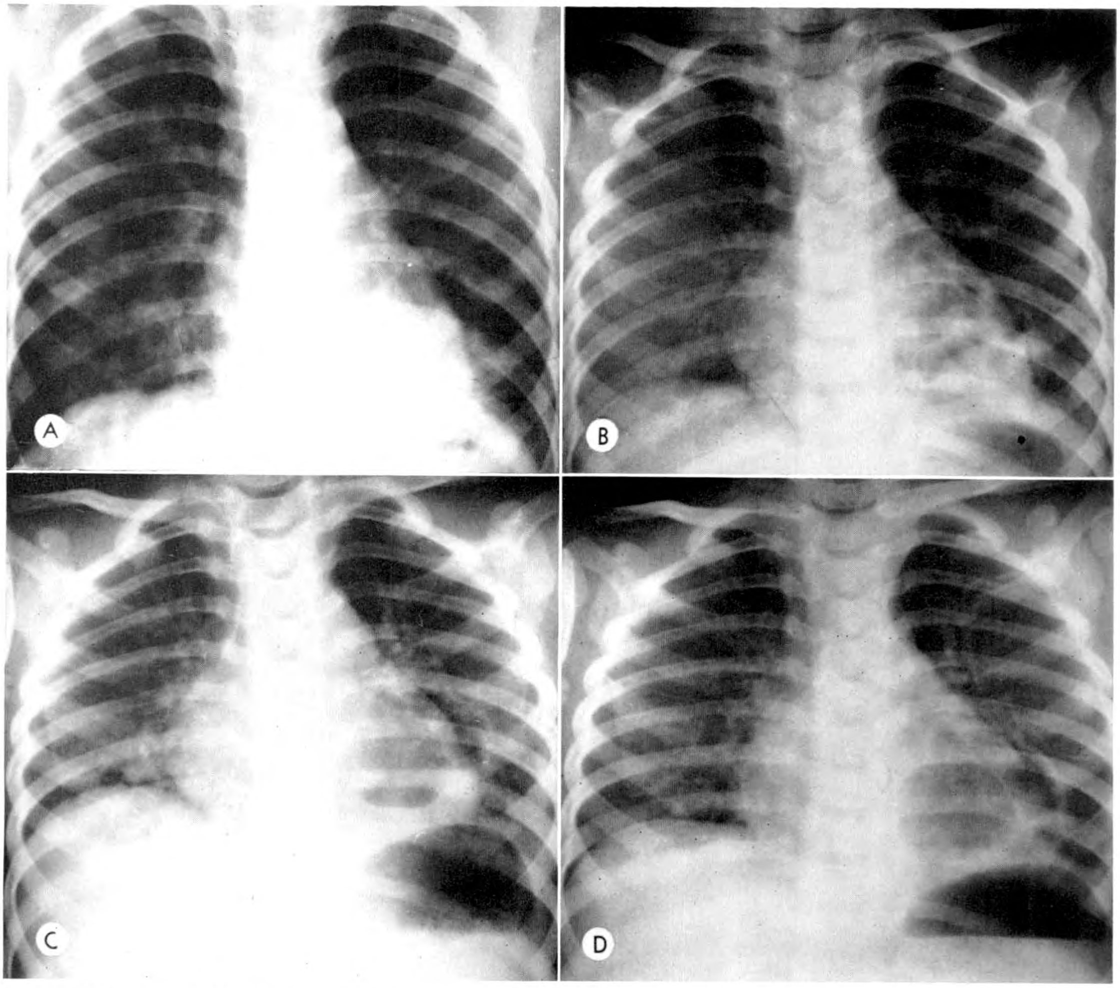

Fig. 1. Case I. (*A*) *April 7, 1959:* Anteroposterior roentgenogram of the chest obtained 12 hours after ingestion. Bilateral confluent basilar infiltrations are seen. Note peripheral hyperaeration. (*B*) *April 15, 1959:* Multiple radiolucent areas have developed in both bases 8 days later. (*C*) *April 20, 1959:* Well developed cystic areas are now seen. Fluid levels are present in the pneumatoceles in the left base. Anteroposterior roentgenogram 2 weeks after ingestion. (*D*) *April 23, 1959:* The persistent thin-walled pneumatoceles without fluid levels are seen 3 days later.

days. A chest roentgenogram at this time revealed multiple radiolucent areas in both bases, more pronounced on the left side (Fig. 1*B*). The left basilar lesions coalesced 5 days later to form two large cystic areas; the largest measured 3 cm. in diameter. Both showed fluid levels (Fig. 1*C*). The fluid levels disappeared within 3 days (Fig. 1*D*). Meanwhile, the child remained afebrile. Her white blood cell count was 7,500 with 39 per cent neutrophils and 6 per cent juvenile forms. The nasopharyngeal culture revealed no growth. The pneumatoceles were still evident on discharge from the hospital 20 days after admission. She was subsequently lost to follow-up, but a chest roentgenogram obtained 21 months later demonstrated complete clearing.

Case II. A 21 month old Negro male drank an unknown quantity of "Kan-Kill" 2 hours prior to admission. He gagged and coughed immediately vomiting a small amount. He was promptly brought to the emergency room where gastric lavage was performed.

On physical examination, his temperature was 38°C., his pulse rate 140 per minute, and the respiratory rate was 60 per minute.

Laboratory examination showed a white

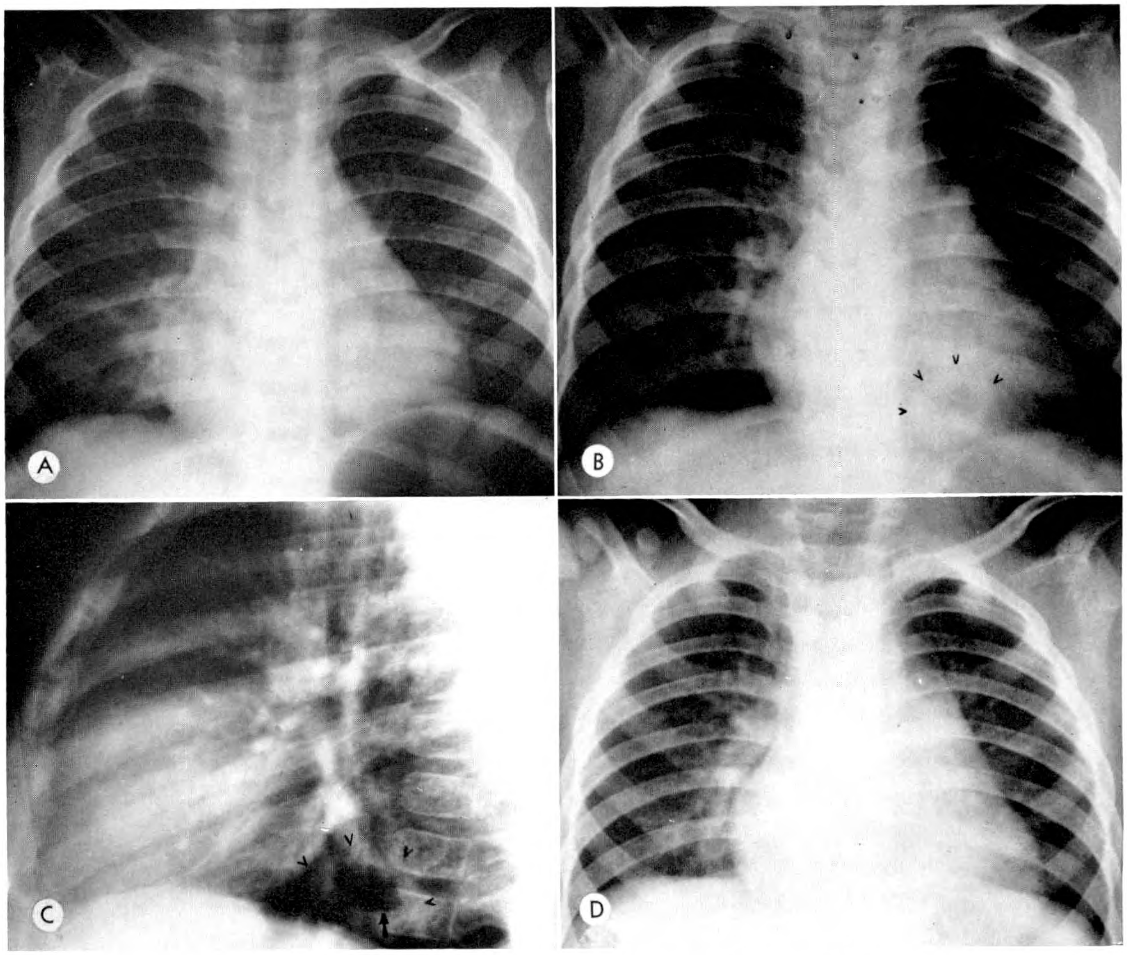

Fig. 2. Case II. (*A*) *March 8, 1960:* Anteroposterior roentgenogram of the chest obtained about 3 hours after ingestion. Bilateral, soft basal infiltrates are noted. (*B*) *March 16, 1960:* Anteroposterior roentgenogram of the chest 8 days later shows a thick walled, 1.5 cm. radiolucency in the posterior basal segment of the left lower lobe (arrows). Partial resolution of the infiltrations is seen. (*C*) *March 16, 1960:* Lateral view shows the fluid level (arrows). (*D*) *March 29, 1960:* Complete resolution demonstrated 13 days later.

blood cell count of 14,250 with 70 per cent neutrophils and 11 per cent juvenile forms. The blood culture was negative. The nasopharyngeal culture yielded a heavy growth of pneumococci. The throat culture showed pneumococci and "normal flora."

The initial roentgenogram of the chest (Fig. 2*A*) demonstrated bilateral confluent basilar infiltrates. These increased slightly during the first day.

The patient was placed in a Croupette with oxygen and steam and started on procaine penicillin therapy. His subsequent course was benign but a roentgenogram obtained 4 days later showed no improvement. His white blood cell count, however, had risen to 30,900 with 60 per cent neutrophils and 6 per cent juvenile forms.

A follow-up chest roentgenogram obtained 2 days later (8 days following the ingestion) demonstrated a 1.5 cm. radiolucency in the posterior basilar segment of the left lower lobe. It was surrounded by infiltration and showed a fluid level better demonstrated in the lateral view (Fig. 2, *B* and *C*). At this time, a nasopharyngeal culture was negative. The patient was asymptomatic; he was afebrile, and his leukocyte count had dropped to 10,850 with 45 per cent neutrophils and 2 per cent juvenile forms. Clinically, the possibility of a lung abscess was entertained nevertheless, and the dosage of penicillin was increased.

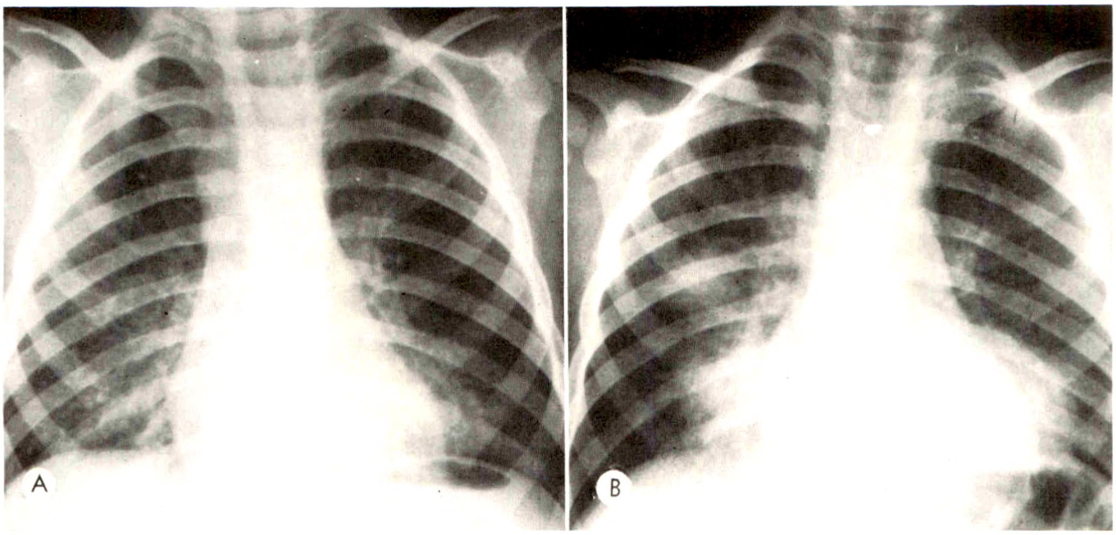

FIG. 3. Case III. (*A*) *September 26, 1963:* Anteroposterior chest roentgenogram obtained 3 hours after ingestion. Bilateral confluent basilar infiltrations are seen. (*B*) *October 1, 1963:* Coalescence of the infiltrations into well defined consolidations is seen. Anteroposterior roentgenogram obtained 5 days later.

Two weeks later, a chest roentgenogram showed complete clearing of the infiltration and of the pneumatocele (Fig. 2*D*).

CASE III. A 2½ year old white male was found to be drinking from a can of "Supertext Paint Thinner" (contains 100 per cent turpentine). Vomiting was induced by the father and the patient was brought to the emergency room 3 hours later where gastric lavage was done.

On physical examination, his temperature was 37.8°C., his pulse was 120 per minute and his respirations were 24 per minute. There was mild subcostal retraction, but the lungs were clear to percussion and auscultation. The initial roentgenogram of the chest showed confluent bilateral basilar infiltrations and peripheral hyperaeration (Fig. 3*A*).

Several hours after admission, the child became dyspneic and his temperature rose to 40°C. His respirations increased to 35 per minute and bilateral coarse basal rhonchi were heard. A roentgenogram of the chest revealed extension of the infiltrative process.

Laboratory data included a white blood cell count of 36,000 with 73 per cent neutrophils and 15 per cent juvenile forms. The nasopharyngeal and throat cultures yielded moderate and heavy growths of pneumococci respectively. The blood cultures were negative.

He was started on penicillin therapy but continued to be febrile. The white blood cell count rose to 40,000.

Roentgenographic examination of the chest 5 days after admission revealed coalescence of the infiltrative densities into well defined rounded consolidations in the bases and in the right upper lobe (Fig. 3*B*). The patient subsequently improved clinically and became asymptomatic. His white blood cell count dropped to 12,500 with a normal differential, but a low-grade fever persisted. The patient was discharged to be followed as an outpatient.

On follow-up examination, 5 days after discharge from the hospital, he was found to be febrile. A roentgenogram of the chest demonstrated radiolucencies within the three areas of consolidation. The largest measured 4 cm. in diameter. Fluid levels were present in the cystic lesions in the lower lobes (Fig. 3*C*). He was, therefore, re-admitted.

On physical examination, at this time, he was found to be irritable and to have a temperature of 38.5°C., a pulse rate of 145 per minute and a respiratory rate of 28 per minute.

The white blood cell count was 12,500 with 40 per cent neutrophils and 6 per cent juvenile forms. Multiple nasopharyngeal, throat and blood cultures showed no pathogenic organism. A moderate growth of *Staphylococcus ablus* was obtained from the nasopharynx.

He was started on intravenous penicillin therapy and became afebrile within 36 hours. On discharge from the hospital, 19 days later, the infiltrations had largely cleared; the fluid levels had disappeared, and the pneumatoceles

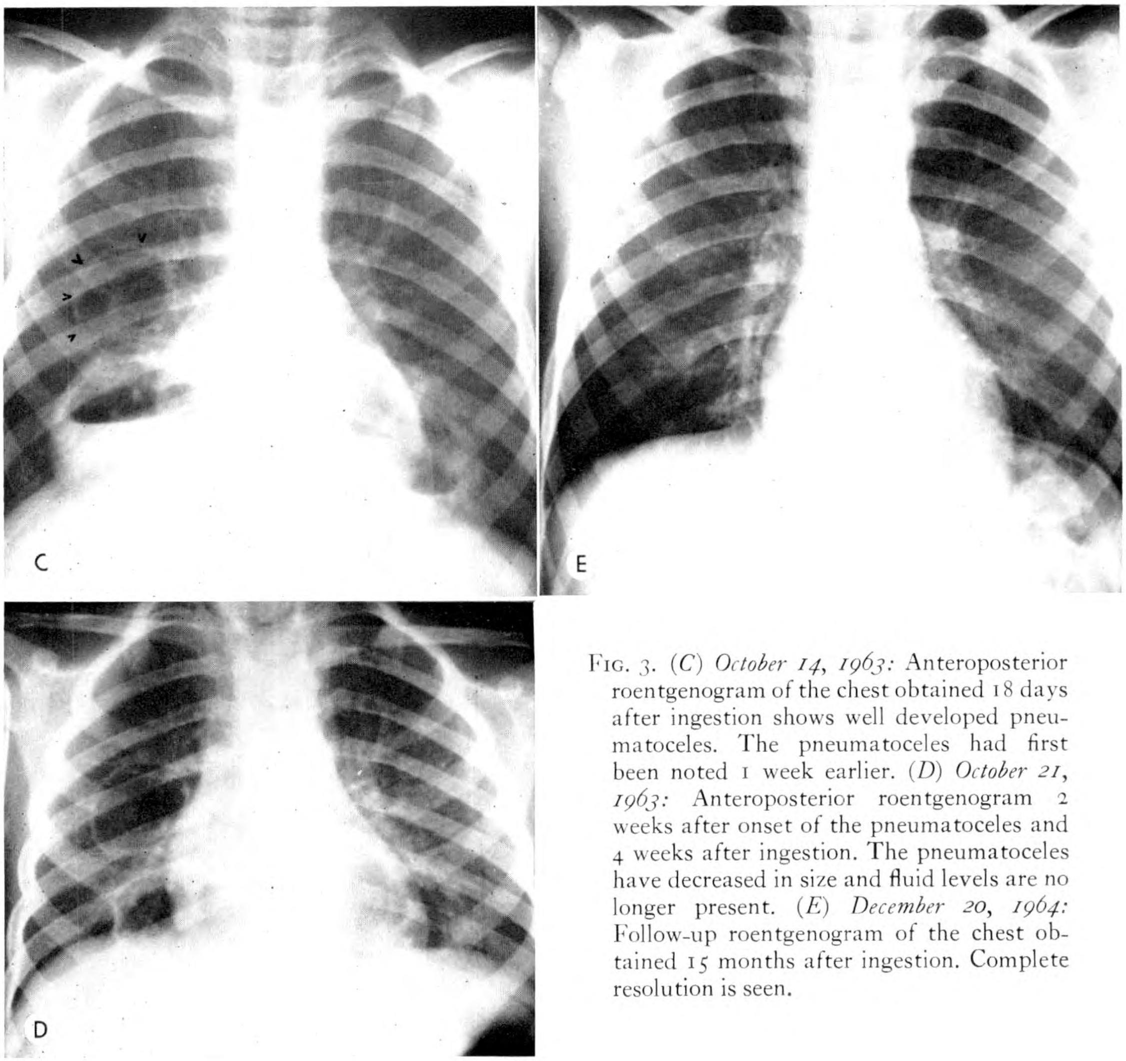

FIG. 3. (*C*) *October 14, 1963:* Anteroposterior roentgenogram of the chest obtained 18 days after ingestion shows well developed pneumatoceles. The pneumatoceles had first been noted 1 week earlier. (*D*) *October 21, 1963:* Anteroposterior roentgenogram 2 weeks after onset of the pneumatoceles and 4 weeks after ingestion. The pneumatoceles have decreased in size and fluid levels are no longer present. (*E*) *December 20, 1964:* Follow-up roentgenogram of the chest obtained 15 months after ingestion. Complete resolution is seen.

had decreased in size and had become thin walled (Fig. 3*D*).

A follow-up roentgenogram 15 days after leaving the hospital demonstrated resolution of the pneumatoceles in the left lower lobe and in the right perihilar area. The pneumatocele in the right lower lobe was still present. It decreased in size on roentgenographic examination 5 months later. The last roentgenogram obtained 11 months following discharge from the hospital revealed no residual abnormality (Fig. 3*D*).

DISCUSSION

Ingestion of petroleum distillates is followed frequently by the development of a characteristic pneumonic infiltration. Pneumonia is estimated to occur in 60 to 80 per cent of all cases.[4,7] In one series, all 21 patients reported developed infiltrations of varying severity.[14] In another group of 149 patients, 65 per cent showed pulmonary infiltrations progressing to consolidation. Of those, over $\frac{1}{2}$ developed infiltrations within 1 hour, and 98 per cent had pneumonia within 12 hours.[7] Pulmonary abnormalities have been demonstrated as early as 15–20 minutes following ingestion.[5,22]

A correlation exists between the amount of hydrocarbon ingested, the severity of the symptoms and the extent of the pulmonary roentgenographic findings.[5] However, amounts of as little as 1 to 2 teaspoons of kerosene have been reported to result in parenchymal infiltrations within 35 to 45 minutes.[8,22]

The mechanism of production of these pulmonary parenchymal infiltrations has been the subject of controversy. The two theories proposed are: (A) that the pneumonia is secondary to aspiration[5,9,18,23,28] and (B) that the pneumonia results from pulmonary excretion of the hydrocarbon absorbed through the gastrointestinal tract.[8,22,26]

The roentgenographic appearance of the resulting pneumonia is rather typical. It is characterized by soft, mottled confluent densities which occur usually in the bases but occasionally extend to the perihilar areas.[5,7] The peripheral lung fields are ordinarily spared but show hyperaeration (Fig. 1*A* and 3*A*).

The typical course is one of relatively slow resolution requiring 2 to 3 weeks.[2,5,14,15,26] Roentgenographic clearing usually lags behind the clinical improvement.[5,14] Very rapid improvement has been reported in occasional cases.[5,7]

In cases of hydrocarbon ingestion, death results from pulmonary edema and overwhelming pneumonia in only a small percentage of cases.[4,8,12,13,15,18,20,22] Nonfatal complications of pneumonia are rare.[10]

Two of the 17 patients in the series of Lesser *et al.*[18] developed pleural effusions; one of them required surgical drainage of the resulting empyema. In the group of Reed *et al.*,[21] one of the 17 patients with pulmonary involvement developed a small effusion on the left side. One of the 60 patients of Bonte and Reynolds[5] demonstrated a pleural effusion, but this was thought to be secondary to a supervening infection.

Pneumothorax and pneumomediastinum complicating nonfatal hydrocarbon pneumonias have also been encountered.[2,25] This complication results from a disturbance in the pressure gradient between the alveoli and the surrounding interstitial tissues in areas of compensatory emphysema with subsequent rupture of alveoli and escape of air into the interstitial tissues.[19]

Subpleural blebs have been noted at autopsy.[8,12] These have been described as small and ranging in size from minute to 1 cm.[12]

The only report of pulmonary cystic cavities developing in hydrocarbon pneumonia that we have been able to find in the English literature is that by Skarbek[26] in 1955. He described a 2½ year old boy who drank a large amount of kerosene. Cysts developed bilaterally in areas of dense basilar infiltration. The largest was 4 cm. in diameter; its wall was about 4 mm. in thickness, and it contained a fluid level. It shrank to about 1 cm. in diameter within 1 week. The process cleared entirely within 2 months. Skarbek concluded that the radiolucencies seen in his case were tension cysts rather than parenchymal breakdown because of the rapidity of recovery and the lack of leukocytic response.

Formation of pneumatoceles is a well known phenomenon in suppurative pneumonia in infants and children. Although more frequently caused by, and identified with, the *Staphylococcus aureus*,[17] it can also be encountered with streptococcus, pneumococcus, Friedländer's bacillus, Proteus organisms,[6] and *E. coli*.[17]

Pneumatoceles are throught to be emphysematous interstitial cavities or cysts.[17] Their formation has been described as resulting from small, coalescing abscesses or areas of necrosis in the interstitial peribronchiolar tissues that follow penetration of the bronchial wall by the invading organism. They eventually perforate into bronchioles and produce an air-containing cavity. If a check-valve mechanism develops, these small cavities can be inflated rapidly and dramatically. Tension cysts of variable size and rapidly changing pattern result.[3,6,11,17,24] Pneumatoceles usually form in the most densely infiltrated areas and may contain shifting fluid levels.[6,24]

Early in their onset, pneumatoceles may be lined with loose granulation tissue. Their

TABLE I

PNEUMATOCELES

		Age	Agent	Amount	Onset of Pneumatoceles	Cyst First Noted	Air-Fluid Level	Laboratory Findings at Onset of Pneumatocele Formation				
								Temperature	White Blood Cell Count	Neutrophils	Culture	Resolution
	Skarbek[23] (1955)	30 mo.	Kerosene	150 cc.	24 hr.	15 da.	Yes	Afebrile	5,000	26%	—	2 mo.
Authors' Patients	Case I (1959)	14 mo.	Petroleum distillate	? ?	12 hr.	8 da.	Yes	Afebrile	7,500	45% (6% juvenile)	NP: negative	21 mo.*
	Case II (1960)	21 mo.	Petroleum distillate	? ?	3 hr.	8 da.	Yes	Afebrile	10,850	4 (2% juvenile)	NP: negative	2 wk.
	Case III (1963)	30 mo.	Turpentine	? ?	4 hr.	11 da.	Yes	38°C.	12,500	46% (6% juvenile)	NP: *S. Albus* Blood: negative	14 mo.

* Lost to follow-up after discharge from the hospital.

walls, however, become progressively thinner as the surrounding pneumonitis resolves and as the cavity enlarges under tension.[6] Pneumatoceles spontaneously disappear after the infection subsides and the bronchiolar obstruction is relieved. They persist for weeks or months after the acute phase of the illness has subsided.[6,11,17] Complete resolution requires an average of 4 months but "in few of the patients they persist indefinitely."[11]

The pathologic anatomy of the lung has been described in a number of fatal cases of hydrocarbon pneumonia.[8,9,12,13,16,18] The predominant findings are those of interstitial infiltrations, hyperemia, capillary endothelial swelling, edema and hemorrhages, bronchiolar necrosis and alveolar exudation. The alveolar exudate has been described as containing a large amount of polymorphonuclear leukocytes.[18]

In view of this histopathologic appearance, one can postulate that the development of a pneumatocele in hydrocarbon pneumonia can occur without an intercurrent bacterial infection. The development of pneumatoceles in our cases, in the absence of clinical evidence of a *de novo* bacterial infection, lends further support to this assumption. An elevated leukocyte count with a shift to the left is known to occur in uncomplicated hydrocarbon pneumonia.[7,13,20,21,25] Furthermore, the leukocyte count had decreased and all the cultures were negative by the time the pneumatoceles had formed in our patients.

The onset of the appearance of pneumatoceles in our patients was within 8 to 11 days following ingestion of the hydrocarbon. Fluid levels were seen within the pneumatoceles in all 3 patients. Resolution required up to 21 months (Table 1).

None of the patients developed additional complications as a result of their pneumatoceles. However, the possibility that these pneumatoceles can expand suddenly or rupture, must be considered. The relative stability of the pneumatoceles in the patients observed may be attributed to the relative absence of the thick secretions that accompany the suppurative pneumonias.

SUMMARY

Three patients who developed pneumatoceles following hydrocarbon pneumonia are reported. The literature on complications occurring in hydrocarbon pneumonitis is reviewed with particular emphasis on tension phenomena and cyst

formation. The pathogenesis, course and prognosis are discussed. All 3 patients progressed to complete recovery without evidence of superimposed infection or additional complication.

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PNEUMOMEDIASTINUM ASSOCIATED WITH ASTHMA AND PNEUMONIA IN CHILDREN*

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THE occurrence of pneumomediastinum during acute episodes of bronchial asthma or bronchopneumonia is a well-known complication. Its actual incidence in children is no doubt considerably higher than the few articles in the literature would indicate. In the present report the roentgen features of this process are emphasized. Since in a previous article[10] the roentgenologic manifestations of spontaneous pneumomediastinum in the newborn were discussed, the author will deal primarily with older children in whom asthma or pneumonia is associated. It has been found that the roentgenologic features of this syndrome in older children differ in some respects from the same process in newborn infants.

CASE MATERIAL

In the last 8 years, 9 patients, 6 females and 3 males, with pneumomediastinum complicating bronchial asthma and 3, all males, in whom it occurred during the course of acute bronchopneumonia have been seen at the Children's Clinic. Of these 12 children, 2 had a second episode of pneumomediastinum and one had 2 subsequent episodes; all of these patients were girls with asthma. A total of 16 instances was, therefore, available for study.

Chronic asthma began between the ages of 9 and 36 months (mean age, 20 months) in 6 patients on whom information was available. The mean duration of asthma before pneumomediastinum first occurred was about 7½ years (91 months), with a range of 3½ to 14½ years. The average age of these patients at the time of pneumomediastinum was about 9½ years (112 months). These figures exclude 2 patients in whom asthma was noted for the first time coincident with the occurrence of pneumomediastinum. These 2 children were younger than most of those with chronic asthma, being 2 and 5 years of age. There was no difference in the age of onset or duration of asthma in the children having multiple episodes of pneumomediastinum or those in whom pneumonia complicated asthma. In the latter group was the patient with three episodes of pneumomediastinum, each occurring during acute asthmatic attacks with complicating bronchopneumonia. The 3 male patients with nonspecific bronchopneumonia and simultaneous pneumomediastinum were younger (16, 57 and 81 months) than the majority of the chronic asthma patients, but the significance of this is impossible to assess. No recurrences were seen in this group.

ROENTGEN FINDINGS

Roentgenographic examination was performed in the supine position in the younger patients (less than 5 years old) and in the erect position, if possible, in the older children.

Mediastinal emphysema, as shown in the frontal and oblique roentgenograms, was seen in the left paracardiac area adjacent to the pulmonary artery in two-thirds of the cases. This usually took the form of streak-like air deposits, although, when there was a large amount of air in the mediastinum, it tended to accumulate in this area rather than in other areas and produced a more homogeneous collection. Equally as common was a superior paravertebral location of the process, frequently bilateral. Other common sites were the carinal and central parabronchial regions, adjacent to the right heart border or between the pericardium and the diaphragm. Over one-half of the cases showed the displaced mediastinal pleura as a linear density, usually on the left side. Air under the thymus could be seen in one-fourth of the cases (Fig. 1, *A* and *B*).

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In the lateral projection, the most common location of emphysema was anterior to the heart, being seen here in 10 of the 16 cases. In three instances there was significant posterior displacement of the heart. Linear accumulations of gas in the middle mediastinum in the region of the esophagus, trachea and pulmonary blood vessels were also seen frequently. The anterior and inferior surfaces of the thymus were outlined by air in over one-half of the cases (Fig. 2, *A*, *B* and *C*). Whether the thymus was thus shown or not seemed to depend on the amount of air which was present; it was always delineated when at least a moderate amount of emphysema was demonstrated. No apparent difference in the appearance of the thymus was seen in the patients who had been on long-term adrenal steroid therapy. The air usually appeared in linear streaks except in the area anterior to the thymus, where homogeneous accumulations could at times be noted.

Subcutaneous or interstitial air was demonstrated outside the confines of the mediastinum in 13 of the 16 cases. The most common locations were the supraclavicular areas and the region of the thoracic inlet. With large amounts of subcutaneous air, the lateral thoracic, presternal and more remote areas were also involved, but this was unusual. Pneumothorax was not detected in any of the patients at any time, nor was pulmonary interstitial emphysema ever demonstrated.

Accurate determination of the length of time required for the absorption of the mediastinal air was not possible as frequent serial examinations were not performed. The earliest complete clearing of a substantial amount of air was seen 7 days after the first roentgenograms were made in 2

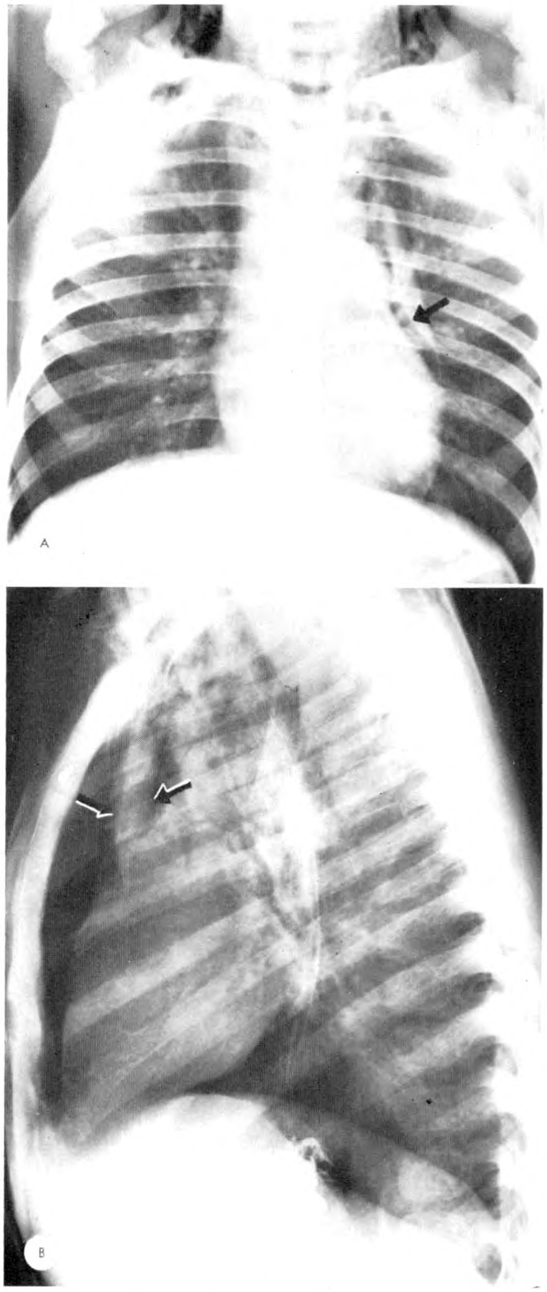

FIG. 1. Five year old boy with pneumomediastinum complicating asthma of recent onset. (*A*) Frontal projection. Both mediastinal pleurae are slightly displaced. Air has accumulated under the thymus (arrow) and in the superior paravertebral areas. Supraclavicular and thoracic subcutaneous emphysema is present. (*B*) Lateral projection. The thymus is outlined (arrows). Substernal air displaces the heart posteriorly. Lamellar air collections in the peri-esophageal region extend into the neck.

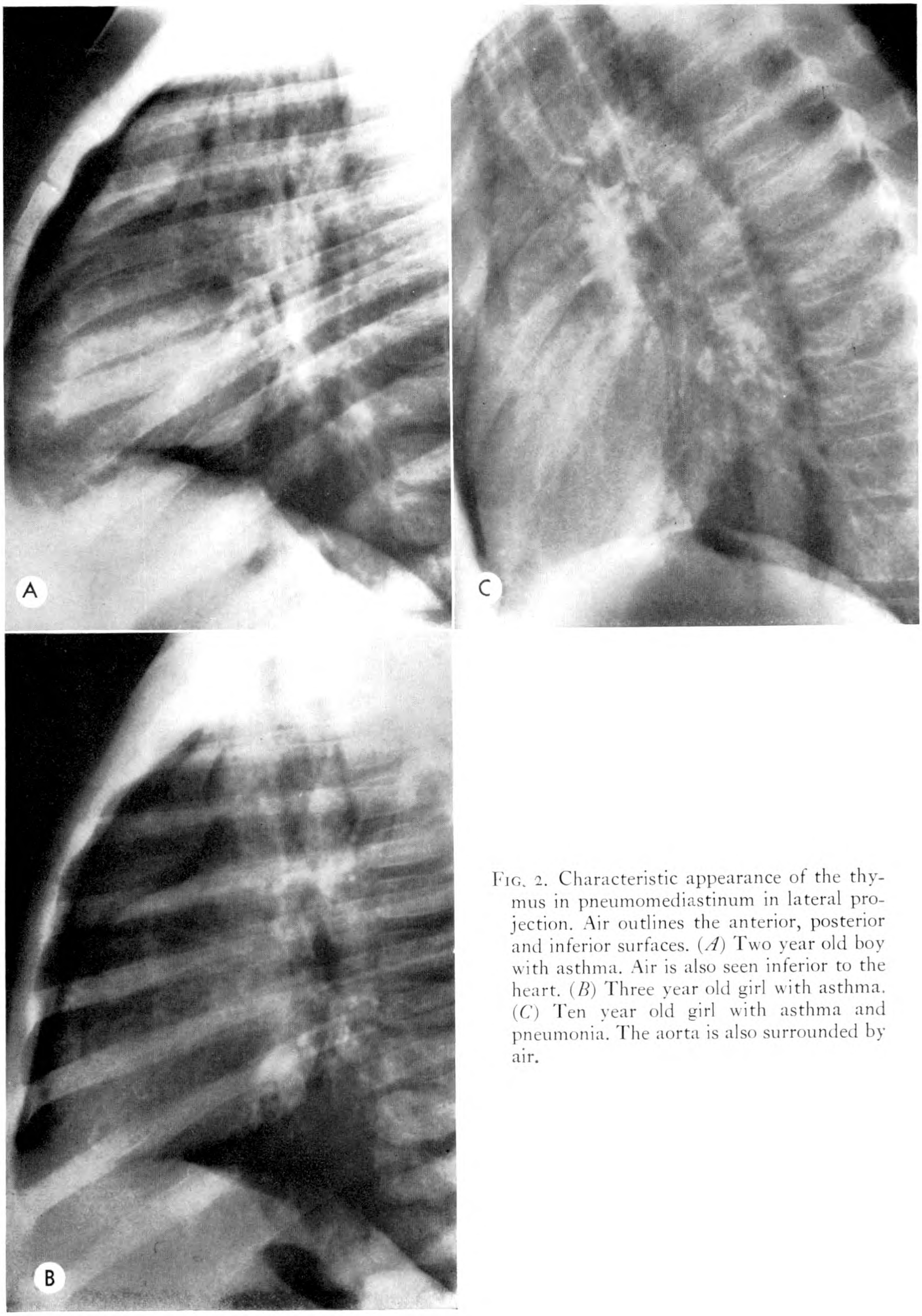

FIG. 2. Characteristic appearance of the thymus in pneumomediastinum in lateral projection. Air outlines the anterior, posterior and inferior surfaces. (*A*) Two year old boy with asthma. Air is also seen inferior to the heart. (*B*) Three year old girl with asthma. (*C*) Ten year old girl with asthma and pneumonia. The aorta is also surrounded by air.

patients, but clearing may have occurred before this. Most cases appeared to be free of gas in about 10 days, an experience similar to that quoted by others.[5,9]

PATHOLOGIC AND CLINICAL FINDINGS

Mediastinal air is assumed to originate with rupture of overdistended alveoli. Overdistention probably occurs following airway obstruction by mucus plugs and bronchospasm in asthma and probably by exudate or inflammatory edema in pneumonia. In addition, the alveolar supporting tissues may be weakened by the parenchymal inflammation in the latter process. Frequent increases in pressure as caused by coughing may also play a part. The released air then takes a centripetal course along the peribronchial tissues. Marchand[4] has noted that the perivisceral fascia enclosing the mediastinal esophagus and trachea extends from the mediastinum over the blood vessels and bronchi down to their third or fourth divisions. The air released by alveolar rupture may pass outside or under this fascia and follow it into the mediastinum. It is evident that once in the mediastinum the air is not confined to this plane exclusively, as much of the air passes anterior to this region and surrounds the thymus. However, some of the air does pass superiorly around the esophagus and trachea, perhaps enclosed in this fascial envelope, and subcutaneous or interstitial emphysema will then result. Inferior passage of the air in the paravertebral or para-aortic spaces, resulting in retroperitoneal emphysema, is less common. Air accumulation in sites similar to those described here was reported by Bariéty and Coury[1] following the induction of artificial pneumomediastinum.

No sex preponderance was noted in this series, which is in agreement with the findings reported earlier.[5,9] There were no fatalities during the episode of pneumomediastinum, although 1 patient died several years later while in status asthmaticus. Norman[7] found 2 fatal cases out of 30 reviewed from the literature.

The mean duration of chronic bronchial asthma before the first occurrence of pneumomediastinum of 7½ years in the present cases compares with an average duration of 2½ and 4 years given by others.[3,5] The average age of these patients at the time of mediastinal emphysema (9½ years) is in general agreement with that in previous reports.[3,5,9] The occurrence of mediastinal emphysema with the first episode of asthma is not usual; a similar experience is reported in another review.[9]

Mediastinal emphysema associated with pneumonia is a well-known entity, having been described with many types of specific and nonspecific lung infections. The 3 cases described here were younger than the patients with longstanding asthma, in general. In 4 cases pneumonia and asthma were both present at the time of pneumomediastinum. McNicholl[6] has reported mediastinal emphysema in siblings with nonspecific and measles bronchopneumonia.

PNEUMOMEDIASTINUM IN NEWBORN INFANTS AND IN OLDER CHILDREN

While in many respects the appearance of mediastinal emphysema in the older children with asthma and pneumonia is similar to that of newborns, marked differences, in which anatomic distinctions between the two age groups may play a part, exist.

There appeared to be much greater air accumulation in the mediastinum of the neonatal infant in relation to body size than in the older child, resulting in marked bulging of the pleurae and obvious elevation of the thymus (Fig. 3, *A* and *B*). In addition, air seemed to coalesce more in the young child; a homogeneous accumulation was seen in all but 1 of 40 cases previously reviewed.[10] In the older child the tissue planes appeared to be more difficult to separate so that air remained in lamellae rather than in large collections.

In marked distinction to the apparent ease of separation of the mediastinal tissue planes in the infants was the fact that some difficulty was evidently encountered in the

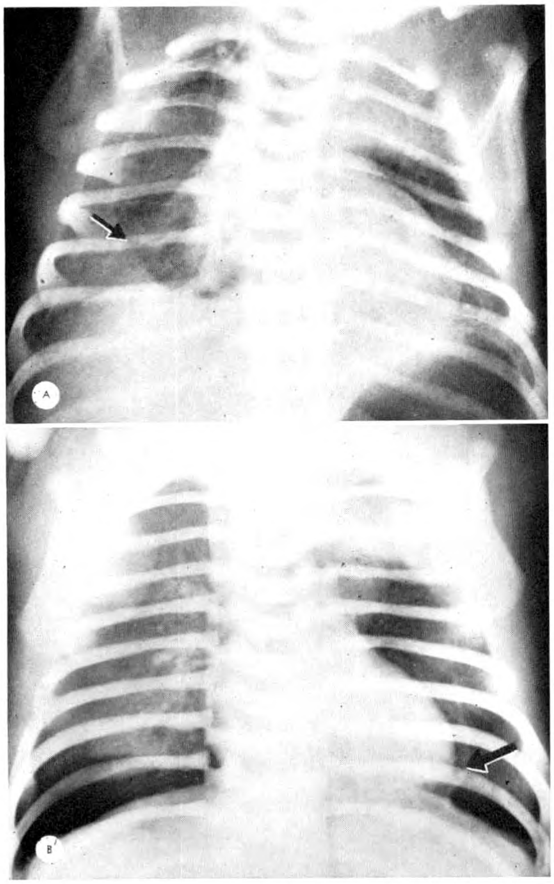

FIG. 3. Marked mediastinal distention in the newborn without subcutaneous emphysema. (*A*) Newborn male. Displacement of right mediastinal pleura (arrow) by spontaneous pneumomediastinum. Right pneumothorax shown later. (*B*) Newborn male. Displacement of left mediastinal pleura (arrow). Bilateral subpulmonary pneumothorax.

mediastinal air breaking through the thoracic inlet and into the interstitial and subcutaneous tissues of the neck. In only 7 of 70 (10 per cent) newborn infants with pneumomediastinum and/or pneumothorax was air present in the subcutaneous or interstitial tissues of the neck, whereas this was demonstrated in 13 out of 16 (81 per cent) of the older children in the presently reported series. It is probable that the escape of a relatively large amount of air into the mediastinum combined with the difficulty in decompression of the air from the mediastinum into the tissues of the neck accounts for the marked mediastinal distention seen in the neonates. This distention resulted in the occurrence of pneumothorax, presumably due to rupture of the mediastinal pleura. Over 60 per cent (25/40) of these infants had a pneumothorax associated with the pneumomediastinum. Moreover, in the previous study 30 patients were observed with pneumothorax alone, many of whom were presumed to have had mediastinal emphysema previous to this. Conversely, the older children with asthma and pneumonia, in whom the mediastinal air was decompressed rather easily into the neck, showed no pneumothorax on initial or serial examination.

The distinction between newborn infants with pneumomediastinum, 60 per cent of whom had an associated pneumothorax, and the older children, none of whom had a pneumothorax, was also noted by others. Evans and Smalldon[2] reported that 3 of 6 newborns with mediastinal emphysema had associated pneumothorax, and only 1 of 6 of the patients with asthma and pneumonia had a pneumothorax. Another group[5] described no instance of pneumothorax in 20 cases of asthma with pneumomediastinum. Pneumothorax is said to occur only occasionally in adults following a diagnostic pneumomediastinum.[1]

The contention that air enters the pleural space after passing through the mediastinum is based on the assumption that air does not usually perforate the visceral pleura of the lung directly.[8] This mechanism may not be applicable in all cases, however. It is also assumed that the mechanism of alveolar rupture with air-tracking into the mediastinum is similar in both the newborn and the older child with asthma or pneumonia; only the cause for the airway obstruction is different.

The difference in the two groups then lies in the route through which the air in the mediastinum is decompressed. It is possible that there is some difference in the anatomic integrity of the tissues at the thoracic inlet, with those of the small infant being more resistant to separation than those of the older child. Decompression would then be more likely to take place through rupture of the mediastinal pleura, if this were an area of less resistance.

Another factor may also add to the differences between these two groups. During roentgenography, the older child is usually sitting or erect, even when symptoms are severe. The mediastinal air thus is in a favorable position to rise into the neck. The newborn infant, however, is usually in a recumbent position and the air is less apt to enter the neck unless this is an area of less resistance. The relative importance of the anatomic and positional factors is unknown, but it is likely that each does influence the course of the disease.

SUMMARY

Sixteen instances of pneumomediastinum in children associated with bronchial asthma or bronchopneumonia were analyzed. The asthma group, comprising 9 of the total of 12 patients, was characterized by a history of asthma starting around 2 years of age and an average duration of asthma, before pneumomediastinum occurred, of $7\frac{1}{2}$ years. The mean age of these patients at the time of pneumomediastinum was $9\frac{1}{2}$ years. The patients with pneumonia only were generally younger.

The distribution of the mediastinal air was similar to that found after diagnostic pneumomediastinum, being noted most often in the left paracardiac, superior paravertebral, perithymic and precordial areas. Extension of the air to the cervical tissues was common. No pneumothorax was noted.

A distinct difference in the manner in which the pressure of the mediastinal air was relieved was noted in the older children when compared to a previously studied group of newborn infants with pneumomediastinum. Decompression in the older children is evidently accomplished through the thoracic inlet tissues; in the newborns there appears to be resistance to this, and consequently the incidence of pneumothorax due to rupture of the mediastinal pleura is quite high. This apparent difference in the course of the disease, evidently due to both the age and the posture of the child, explains the dissimilarity in the roentgen patterns for the same process in the two age groups.

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CAVITARY PULMONARY LESIONS FOLLOWING NONPENETRATING CHEST TRAUMA IN CHILDREN*

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INJURY to the underlying pulmonary parenchyma occurs commonly in major nonpenetrating chest trauma. In 2 large series pulmonary contusion was noted more commonly than rib fractures. In Williams and Bonte's[15] series of 150 cases, 58 per cent had visible rib fractures, while 72 per cent had pulmonary contusions, and in Westermark's[14] series of 124 cases, 45 per cent had rib fractures, while 75 per cent had changes of pulmonary contusion.

According to Williams and Bonte,[15] the more uncommon lesions associated with nonpenetrating chest trauma include atelectasis, interlobar hematoma, emphysema, lung torsion, and lung hernia. More commonly, these traumatic pulmonary changes can be divided into 3 main entities which can either occur separately, coexist, or evolve one from another.

Of the 3, pulmonary contusion occurs most commonly and is seen roentgenographically as either an area of homogeneous infiltrate secondary to alveolar exudation of fluid or as a stringy interstitial infiltrate, probably representing peribronchial and perivascular hemorrhage. These changes are seen soon after injury and usually clear within days.

A pulmonary laceration is seen as a cavitary lesion, often containing an air-fluid level, surrounded by a variable amount of consolidation. These areas probably represent a tear in the pulmonary parenchyma with leakage of air and fluid into this tear. They resolve in an average of 6 weeks or are replaced by a hematoma.

Intrapulmonary hematoma is the third category. These lesions appear as either rounded or elliptic solid densities which may contain a small crescentic air shadow at their superior border, arising within an area of pulmonary contusion or laceration. They resolve in an average of 17 weeks.

We feel that it is frequently difficult to categorize these pulmonary parenchymal changes and in some cases it may be preferable to describe the roentgenographic changes present, remembering that the pathology is secondary to nonpenetrating injury.

The purpose of the authors is to describe an unusual manifestation of chest trauma in children and to point out the desirability of conservative management of these patients. The following are examples of pulmonary consolidation with cavity formation occurring almost immediately after blunt trauma to the chest. A remarkable feature of these cases is the benignity of the clinical course.

REPORT OF CASES

CASE I. A 5 year old boy, who had been in good health without previous history of a respiratory illness, was seen at the Emory University Hospital emergency room on January 12, 1963 because a large flower pot weighing 150 to 200 pounds had fallen on his head and posterior chest. He was unconscious for 2 to 4 minutes following the accident and when first seen by his mother was mildly cyanotic with rattling respirations. The patient was examined within 1 hour in the emergency room at which time he was conscious and well oriented. The blood pressure was 115/50, pulse 120, respirations 22 and grunting in nature, and temperature 99.5° F. rectally. Physical examination showed a well developed boy who had a large hematoma over the right forehead and a small abrasion over the posterior back at the T8 level. Other pertinent findings included rales and rhonchi heard throughout the chest and a normal neurologic examination.

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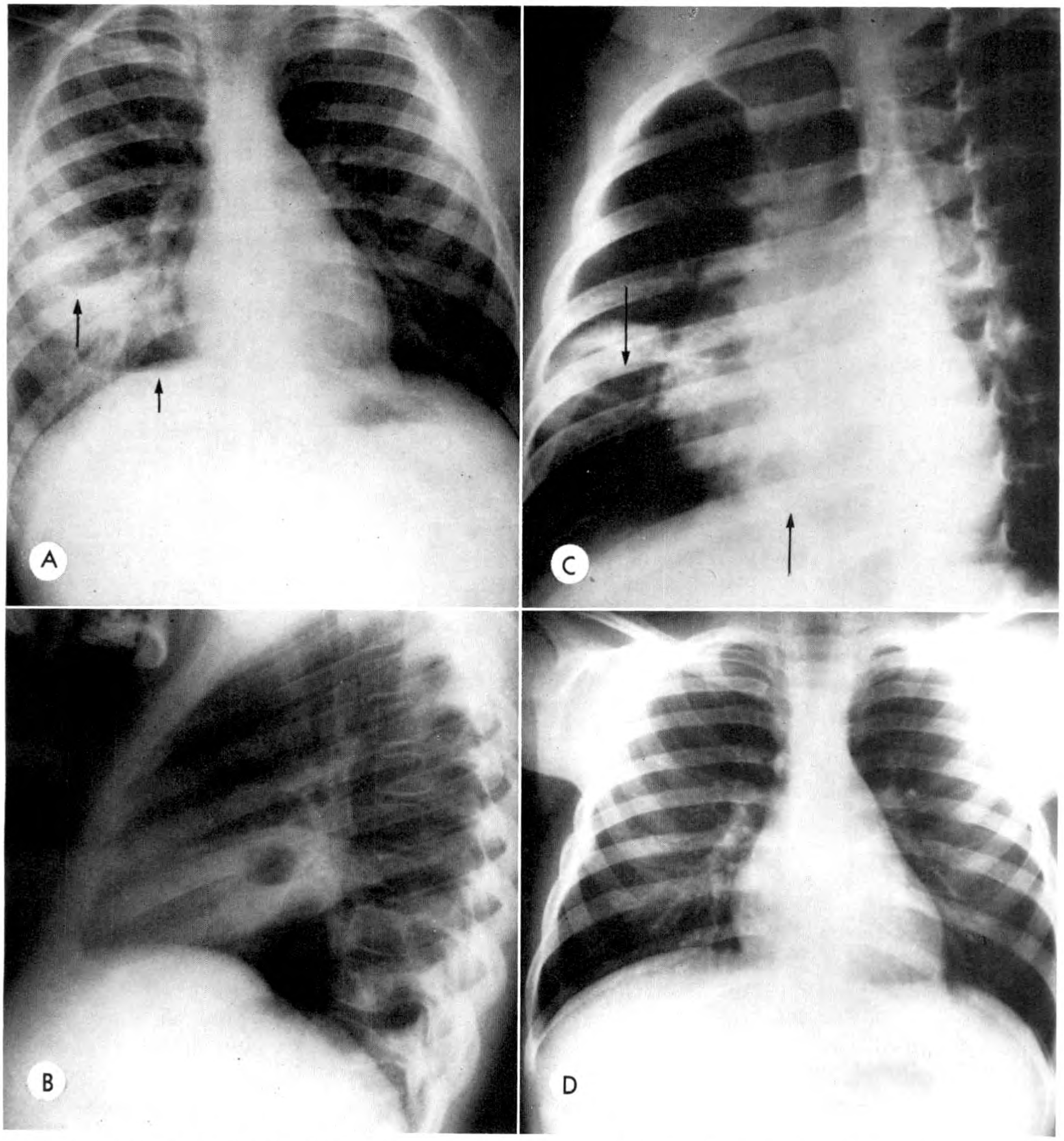

Fig. 1. Case 1. (*A*) Initial frontal roentgenogram showing air fluid levels in cavitary lesions (arrows) with surrounding hazy infiltrate. (*B*) Lateral view at 2 days shows a cavitary lesion and dense consolidation in the middle lobe. (*C*) Right posterior oblique view showing the mildly cystic appearance of the middle lobe lesion (upper arrow) and vaguely seen right lower lobe cavity at 2 days (lower arrow). (*D*) Normal appearing frontal view except for periosteal reaction along the right lateral seventh rib as the first evidence of rib fracture at 11 weeks.

Skull roentgenograms were normal. Chest roentgenograms showed a generalized, hazy, increased density over the right lower lung field containing two cystic cavities with air-fluid levels (Fig. 1*A*). The largest cavity measured 2×2.5 cm. and was seen in the area of the middle lobe, and the second measured 2 cm. across in the right lower lung field posteriorly. Shortly after the chest roentgenograms were taken, the patient vomited and coughed up a small amount of blood-tinged material.

He was hospitalized and placed on procaine penicillin 600,000 units per day. On the following day the chest was clear to auscultation and the patient was asymptomatic. The chest roentgenogram 2 days following the injury showed general clearing of the pulmonary consolidation except in the lateral segment of the right middle lobe where the density had inincreased (Fig. 1*B*). The thin walled cavity seen in the middle lobe had decreased to a diameter of 1.5 cm. and the air-fluid level was no longer seen. The cavitary lesion in the posterior segment of the right lower lobe was seen only on the right posterior oblique Bucky roentgenogram, which also showed that the middle lobe cavity was multilocular (Fig. 1*C*). Evening rectal temperatures were 99.8° F. while morning temperatures were as high as 101.2° F. until the sixth hospital day, after which all temperatures were normal. Nine days after the initial injury chest roentgenograms showed poorly defined margins of the lucent area in the middle lobe with a moderate decrease in the consolidation in this area. The lower lobe appeared normal with no evidence of the previously demonstrated cystic cavity.

The patient was discharged, still asymptomatic, on January 23, 1963. On January 28, 1963, 16 days after the injury, the remaining cavitary lesion in the middle lobe had disappeared and a 2 cm. area of consolidation located just posterior to the original area of cavitation was all that remained. Eleven weeks later, the chest appeared normal except for some periosteal reaction along the right seventh rib laterally as the first and only evidence of rib fracture (Fig. 1*D*).

Case II. A 9 year old male, who had previously been in good health, sustained moderately severe blunt trauma to the right side of the chest in an automobile accident. The patient was brought to the emergency room of Grady Memorial Hospital immediately following the accident where examination was normal except for superficial abrasions over the right anterior chest.

The initial chest roentgenogram obtained approximately 90 minutes following the trauma revealed a fairly small area of hazy density over the right mid lung field in the center of which was an oval lucent area measuring 2×1 cm. in diameter, seen best in the right posterior oblique view (Fig. 2*A*). The left lung was normal. The roentgenographic impression was lung contusion with central cavity or pneumatocele formation.

As the patient was asymptomatic, he was observed as an outpatient with no specific treatment until the morning of the third day when he awoke with shortness of breath and right sided pleuritic chest pain. He was admitted to the hospital where physical examination and temperature were again within normal limits. Laboratory studies included negative throat and blood cultures and normal blood cell count. The second chest roentgenogram obtained at this time, 3 days after the initial accident, revealed a slight increase of the density in the right lower lobe with the central lucency remaining unchanged (Fig. 2*B*). Again, the left lung field was clear. Subsequent to the patient's episode of shortness of breath and pleuritic chest pain, he became rapidly asymptomatic on no therapy with no evidence of infection and after discharge remained in good health. He was last seen in the outpatient clinic approximately 19 days after the accident and was completely well. A chest roentgenogram obtained on that visit revealed virtually complete clearing of the lung density with no remaining trace of the cavity (Fig. 2*C*).

Case III. A 4 year old Negro boy, who had no previous history of respiratory tract difficulty, fell from the bumper of his father's truck on November 25, 1957. The wheels of the truck passed over his chest. Immediately afterward he was asymptomatic with no evidence of dyspnea, chest pain, or hemoptysis. Because of the nature of the injury, a chest roentgenogram was obtained which showed a hazy increase in density in the right mid and upper lung fields with a cavitary 1.5×1 cm. rounded lesion near the right hilus which contained a prominent air-fluid level. A poorly defined rounded area of radiolucency was also present in the right upper lung field (Fig. 3*A*). The patient remained asymptomatic, but because of the roentgenographic findings he was seen again the following day. Temperature, pulse, respirations, and white blood cell count were normal and the chest roentgenogram was unchanged.

An examination obtained 2 weeks following the injury showed clearing of the hazy density with coalescence of the previously described pulmonary cavities into one multilocular cystic lesion. The air-fluid level was no longer present and a fracture of the left first rib was seen (Fig. 3, *B* and *C*). Examinations at 4 and 7 weeks showed diminution in size of the cavities and a roentgenogram at 11 weeks was within normal limits (Fig. 3*D*). During this period of time the

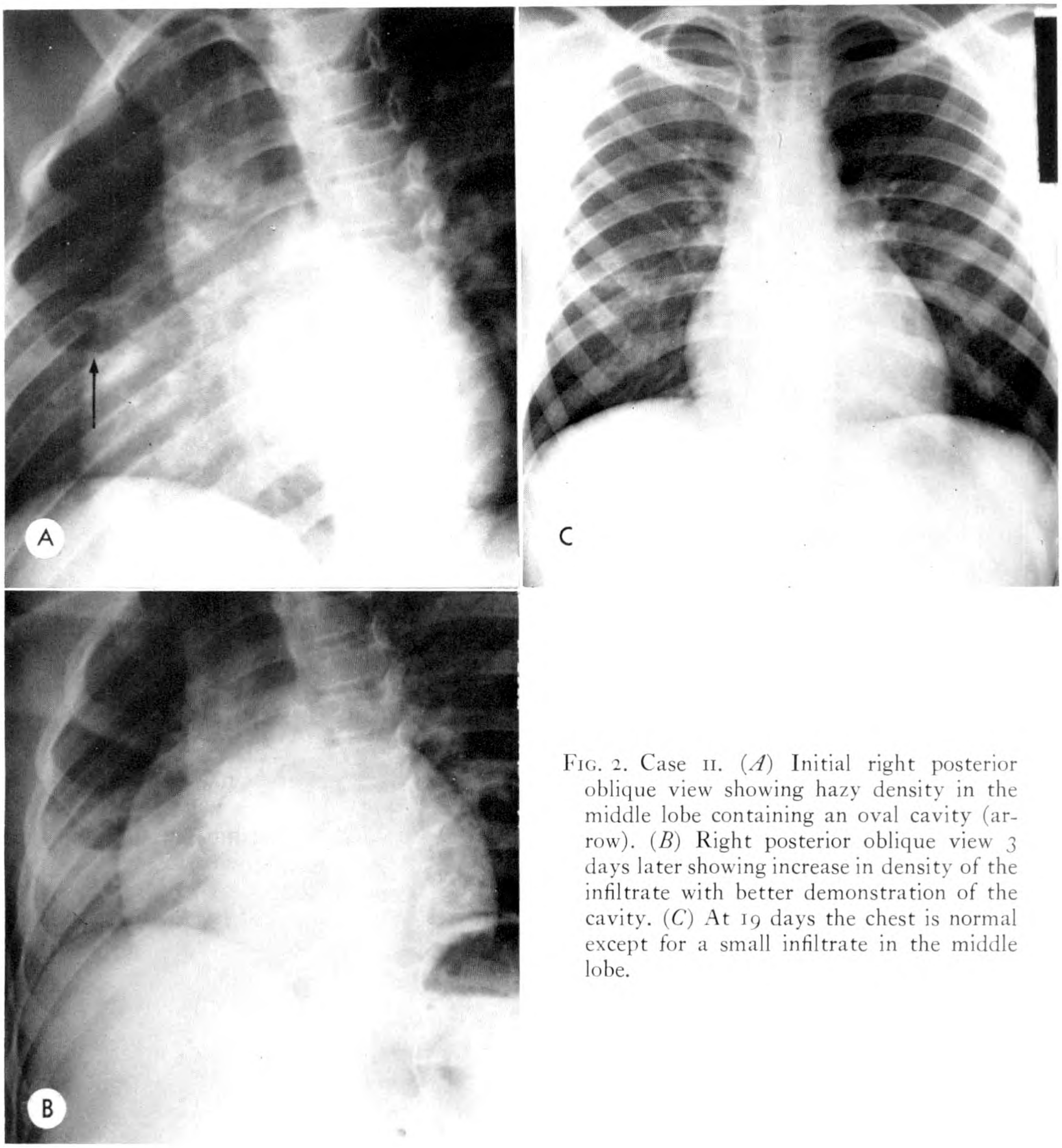

Fig. 2. Case II. (*A*) Initial right posterior oblique view showing hazy density in the middle lobe containing an oval cavity (arrow). (*B*) Right posterior oblique view 3 days later showing increase in density of the infiltrate with better demonstration of the cavity. (*C*) At 19 days the chest is normal except for a small infiltrate in the middle lobe.

child remained asymptomatic and no treatment was given.

COMMENT

There have been 25 reported cases[2–9, 11–13,15] of cavitary pulmonary lesions following nonpenetrating chest trauma and of these 20, or 85 per cent, occurred in the patients under the age of 30, more commonly in males, perhaps relating both to the more resilient chest cage of younger people and the type of trauma incurred in this younger age group.[3]

Three cases have been described in children 15 years or less in age. Greening *et al.*[6] reported the case of a 6 year old female who sustained multiple rib fractures after falling from a horse. A chest roentgenogram 2 hours later showed consolidation in the right mid lung field within which was a thin walled cystic lesion. During the next 2 days, the consolidation became more defined and

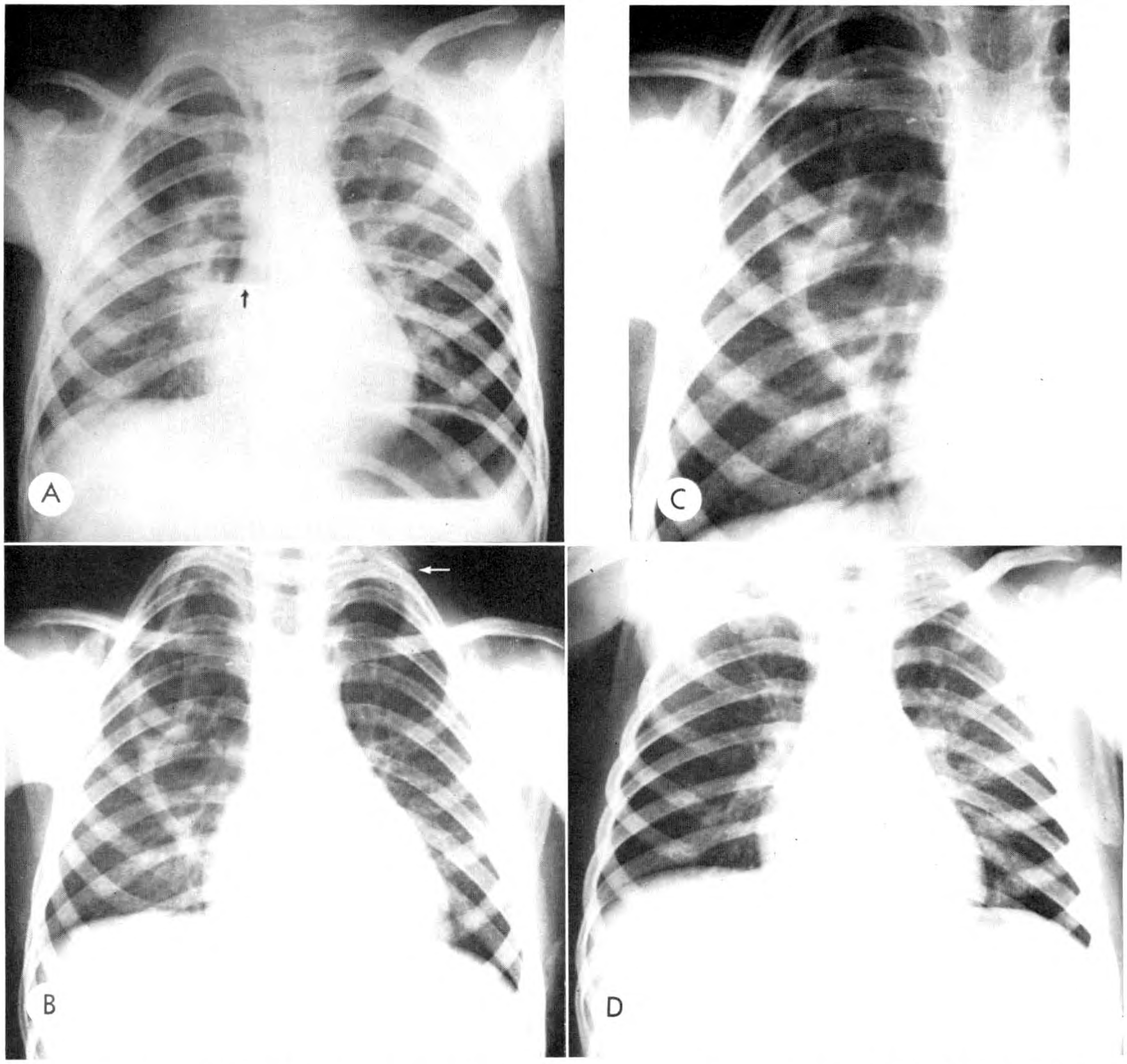

FIG. 3. Case III. (*A*) Initial roentgenogram showing hazy increase in density in the right mid and upper lung fields with a cavitary lesion near the right hilus containing a prominent air-fluid level (arrow) and a poorly defined lucency in the right upper lobe. (*B*) Coalescence of the cavitary lesion into one large multicystic lesion at 2 weeks. Also a fracture of left first rib is present (arrow). (*C*) Close-up view of multicystic cavity. (*D*) Normal appearing chest at 11 weeks.

the cystic lesion increased somewhat in size. At 10 days the lesion had decreased in size and in 3 months the chest appeared normal.

Schwartz and Borman[12] reported an 8 year old boy who fell from a height of 5 meters. A chest roentgenogram $1\frac{1}{2}$ hours later revealed a pneumomediastinum and an area of consolidation in the left lung field which contained a lucent area with an air-fluid level. The patient was placed on antibiotic therapy and discharged on the 8th day when the only roentgenographic abnormality was a residual ring shadow 2 cm. in diameter.

Joynt and Jaffe[7] included in their reports an 8 year old boy who suffered head and chest injuries in an automobile accident. He was unconscious for a few hours, then coughed up a small amount of frothy, bloody sputum. An initial chest roentgenogram showed patchy infiltrate in the right lung and a small pneumothorax. Two days later the infiltrate had increased and a ring shadow suggesting cavity formation appeared. On the 7th day the chest roentgenogram appeared normal but on a follow-up examination at 8 weeks, a well circumscribed opacity in the region of the previously demonstrated ring shadow had appeared. This opacity disappeared during the next 3 months.

As compared to the cases occurring in adults, the childhood cases showed no significant differences in either the clinical or roentgenologic features.

CLINICAL FINDINGS AND TREATMENT

In the 25 previously reported cavitary pulmonary lesions associated with blunt trauma, including all ages, hemoptysis was the most constant clinical finding occurring in 14 cases. Hemoptysis varied from a small amount of blood streaked sputum seen shortly after injury to the coughing up of dark red blood clots daily for as long as 10 days following injury. Hemoptysis may be delayed until the second to fifth day. Other symptoms included minimal cough, chest pain and dyspnea, usually only on the first day. Mild temperature elevation and leukocytosis have been reported, probably related to reabsorption of blood products. Infection has rarely become clinically evident.[4,6]

We feel, as do others,[2,3,6,8] that in most cases prophylactic antibiotics are not indicated. Purulent sputum and an increase in pulmonary consolidation after the fifth or sixth day, as seen roentgenographically, along with increasing temperature and leukocytosis, are evidence of superimposed infection. Treatment should be symptomatic and dictated by the severity of the associated injuries.

ROENTGENOGRAPHIC FINDINGS

In general, these cavitary lesions are poorly delineated with a prominent air-fluid level initially and are seen within hours or during the first few days following injury. They are usually present in an area of hazy, cloudy, alveolar type pulmonary consolidation which during the first few days may decrease or increase in size and density. By the end of 7 to 10 days the consolidation has generally disappeared or decreased markedly, and by 2 to 7 weeks the cavitary lesion has resolved. It appears, however, that if the initial cavitary lesion did not contain an air-fluid level and is seen as a single cystic lesion, a pulmonary hematoma may evolve which takes longer to clear, averaging 17 weeks.

Some of these cavitary lesions are multicystic, occurring either initially or during the first 6 days following trauma. They are also associated with pulmonary consolidation but may not contain air-fluid levels and evidently do not evolve into pulmonary hematomas.

There are several entities which may simulate the roentgenographic appearance of traumatic pulmonary cavity formation including the following: pyogenic pulmonary abscess, postinflammatory pneumatocele, pulmonary tuberculosis in older children, pulmonary sequestration and communicating bronchogenic cyst. Other rarer conditions may also produce a similar picture. The differential diagnosis of these cavitary lesions should prove quite easy, provided the patient's history and clinical course are kept in mind. In most instances, the antecedent history of chest trauma and an awareness of this condition on the part of the physician should make the diagnosis obvious.

ETIOLOGY AND PATHOLOGY

Three of the 25 previously mentioned cavitary lesions were surgically removed,[7,11,13] and one was drained.[6] They were soft and cystic, containing dark red to orange products. The wall was apparently derived from the subpleural and interlobar connective tissue and varied in thickness. Microscopically, there were numerous hemosiderin containing macrophages and even some fibrosis in the surrounding tissue.

Because of the rarity of the lesion and because so few pathologic studies have been performed, the pathogenesis remains conjectural. These lesions probably represent a tear or laceration of the pulmonary parenchyma and contain air because of escape from the alveoli and small bronchioles.[15] That the negative intrapleural pressure is important is shown by the experiments of Moolten[10] and Forsee and Blake,[5] who created pulmonary tears in postmortem lungs. In Forsee and Blake's experiment, the lungs were then inflated by evacuating a bell jar simulating the negative intrapleural pressure, and an air-containing rounded lesion appeared which was larger than could be accounted for by actual tissue destruction.

A similar phenomenon was also seen clinically by Beumer and Mellema,[1] who found a 4.7 per cent incidence of cavitary lung lesions following pulmonary segmental resections when 40–100 cm. H_2O pressure was used in draining the pleural space as compared to 0.9 per cent incidence when 8–10 cm. H_2O pressure was used.

SUMMARY

Three cases of cavitary pulmonary lesions following closed chest trauma in children have been presented along with a brief review of the literature. The roentgenographic findings are single or multicystic cavities often containing air-fluid levels, surrounded by a variable amount of consolidation. The clinical picture is, in general, benign with hemoptysis the most common finding. Treatment is usually dictated by associated injuries and prophylactic antibiotics are unnecessary.

These cavitary lesions should not be confused with more common entities, such as lung abscess, as the differential diagnosis can be made by an awareness of the condition, serial roentgenographic findings, and the clinical history.

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THYMIC PATTERNS IN THE NEWBORN*

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A STUDY of 1,020 frontal chest roentgenograms obtained on consecutive newborn infants at Morrisania City Hospital was undertaken in the winter of 1958–1959. The purpose of the study was to determine the frequency of congenital abnormalities in the newborn thorax. The frequency of such abnormalities in this series was surprisingly low (not a single skeletal abnormality was identified). Incidental findings in the heart and lungs will be briefly discussed, but the attention of the authors was directed particularly to the variation in thymic configuration.

GRADING

Prominence of the thymus was graded into 3 stages on either side (1+, 2+, 3+) and correlated with the area of the hemithorax (Table I). The relative frequency of the various grades of thymic prominence is shown in Table II.

In 517 cases of this series (roughly 50 per cent), there was no mediastinal bulge on either side. These cases were coded as Grade 0. It was found that "enlargement" of the right lobe of the thymus occurred with distinctly greater frequency than left lobe prominence. Similarly, the various stages of thymic prominence were more frequent on the right side. In 276 cases (slightly more than 25 per cent of the series), there was thymic prominence on the right side only. Figure 1, *A* and *B* shows Grade 3 prominence on the right and left side, respectively.

VARIOUS PATTERNS

The frequently described "sail sign," a triangular shaped prominence of the superior mediastinal image, is shown in Figure 2. This pattern was encountered in a surprisingly small number of cases (less than 5 per cent of thymic prominences). An undulating contour of the lateral border of the thymus, due to indentations by the anterior rib segments, was found rather frequently in the presence of prominent thymic images (Fig. 3, 4 and 5). A combination of the "sail sign" with undulation of the thymic border is demonstrated in Figure 4. A prominent thymus may occupy the entire width of the thorax or its entire vertical diameter, thereby completely obscuring one or both sides of the cardia silhouette (Fig. 5). We have not encountered extrathoracic extension of the thymus in any direction, although a cervical thymus has been observed by Moseley and Som.[9] We have never seen the lumen of the trachea compressed or displaced by a prominent thymus, regardless of its size or situation.

In a few instances, we were able to observe an interval change in thymic configuration on a follow-up examination obtained for various reasons after 2 to 4 weeks (Fig. 6, *A* and *B*). While in most cases we have noted an enlargement of the thymic image during the first few weeks of life, in a few cases a decrease in the thymus occurred, possibly due to a disease elsewhere in the body which occasioned the roentgenographic examination. It is well known that the thymus decreases under stress and the discharge of steroid hormones. In one instance (Fig. 7), we encountered radio-

Table I

GRADES OF THYMIC PROMINENCE

Grade 0—thymus not visualized
Grade 1—less than 15 per cent of area of hemithorax
Grade 2—15–30 per cent of area of hemithorax
Grade 3—greater than 30 per cent of area of hemithorax

Note: Right hemidiaphragm was noted to be usually at level of 8th rib (posteriorly).

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TABLE II

PATTERNS OF THYMIC PROMINENCE (1,020 CASES)

No prominence on either side	517	
Unilateral Thymic Prominence		
Right side	276	
Left side	75	
Bilateral Thymic Prominence		
Grade	Right	Left
1	109	81
2	169	65
3	117	31

lucent areas within the prominent thymus, suggesting the presence of fatty tissue (lipoma?) in the prominent thymus.

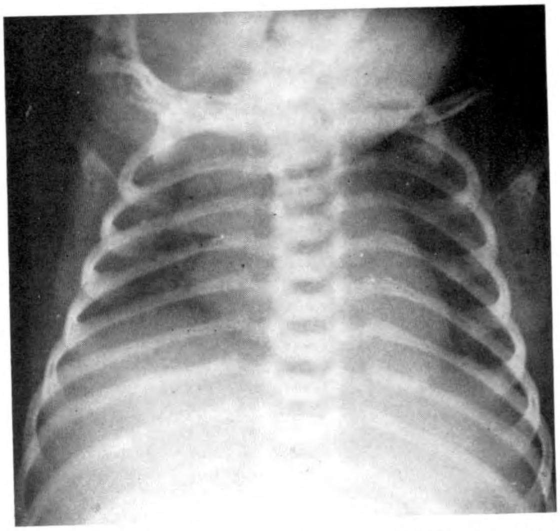

FIG. 2. Right lobe prominence. Roentgenogram shows the "sail" sign. This was encountered in less than 5 per cent of prominent thymic images.

DIFFERENTIAL DIAGNOSIS

Our study was confined to frontal roentgenograms. Certain criteria permit the identification of a mediastinal image as being thymus. According to the silhouette sign, the cardiac border will be obscured by an anterior density. The indentation of the lateral thymic border by anterior rib segments is characteristic of thymus. The "sail sign," when present, will prove to be helpful (although in our experience this has not been a frequent finding, as pointed out above). In certain instances, the thymic prominence has to be differentiated from a pneumonic consolidation. The absence of an air bronchogram, together with the scalloping of the lateral margin, is indicative of thymus. It should be pointed out that an air bronchogram can be encountered physiologically on the medial aspect of each hemithorax, as long as the bronchi are intramediastinal, and that an air bronchogram assumes significance in a more peripheral location. An intrathoracic goiter will almost invariably affect the trachea.

A dermoid tumor, also occurring in the anterior mediastinal compartment, may

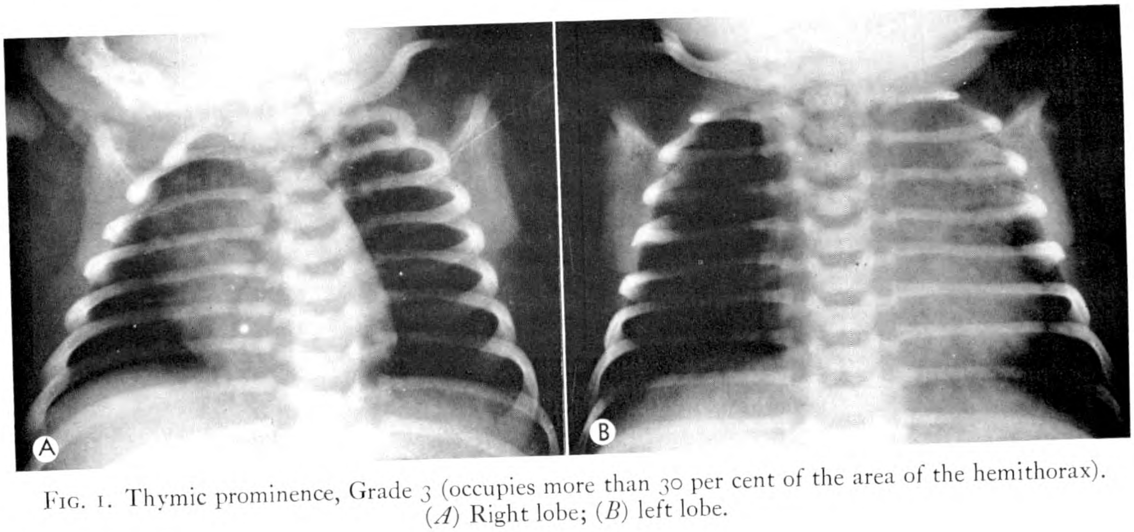

FIG. 1. Thymic prominence, Grade 3 (occupies more than 30 per cent of the area of the hemithorax). (*A*) Right lobe; (*B*) left lobe.

simulate a prominent thymus, but can sometimes be differentiated by virtue of its contents of tooth structures or skeletal parts, as well as the absence of an undulating peripheral contour. Malignant lymphomas, confined to the anterior mediastinum, can be differentiated from the thymus when other mediastinal structures are compressed and/or displaced. Total anomalous pulmonary venous drainage may present prominence of the superior mediastinum, but it will show a constriction at the base of the heart ("snowman" contour) and is not as anterior as the thymus. Confirmation of a mediastinal mass as being thymus can be obtained by administration of steroids, as suggested by Caffey.[2]

INCIDENTAL FINDINGS OBSERVED DURING THIS STUDY

The right horizontal fissure was clearly visualized in 129 cases. This finding is normal and due to the plane of the incident beam in relation to the slight curve and slope of the fissure rather than to any pathologic thickening.

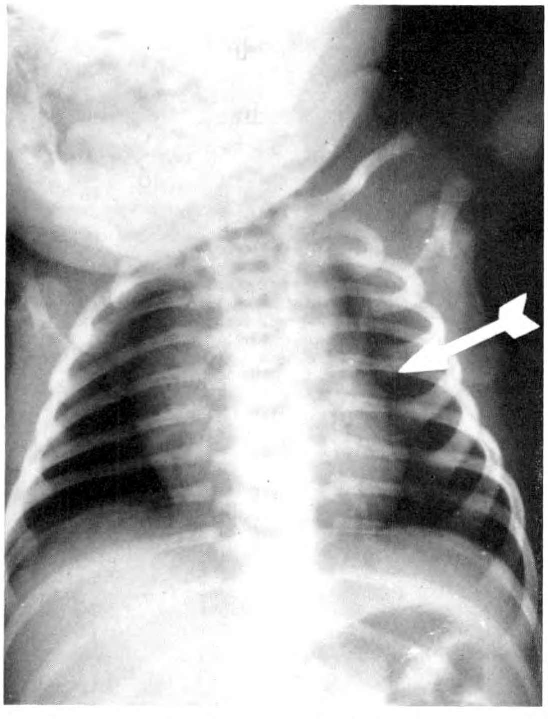

Fig. 3. Scalloping of the left border of a prominent thymic image due to contact with the anterior left rib segment. Such undulation of the border was found to be a most reliable sign of thymic prominence.

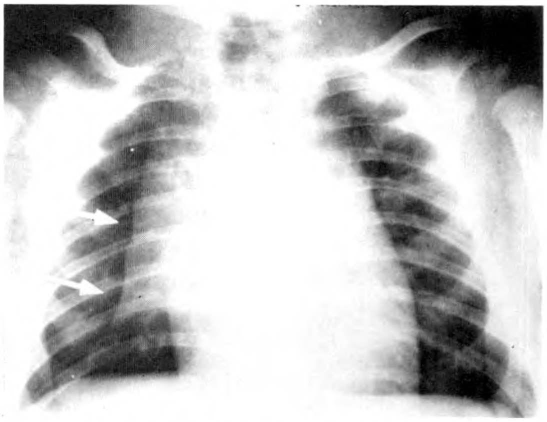

Fig. 4. Prominence of right lobe of thymus. Roentgenogram shows the "sail" sign as well as undulations (arrows).

Skin folds, simulating a pneumothorax, were demonstrated in 51 instances. Skin folds are generally characterized by their extension beyond the confines of the thorax, as well as in atypical directions, which do not conform to the contours of the lung periphery (Fig. 8).

A pneumothorax was seen in 5 instances (Fig. 9). Davis[3] described the vertical fissure line, which has to be differentiated

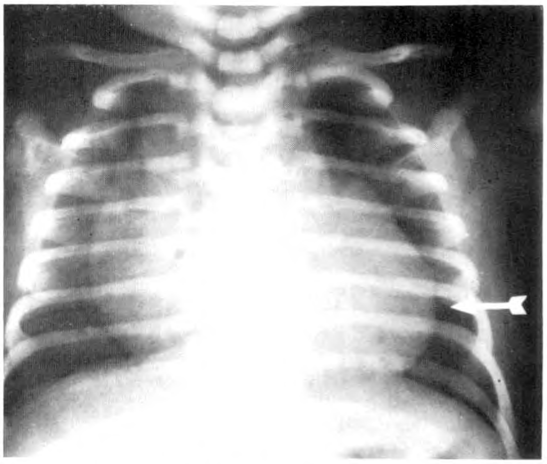

Fig. 5. Prominent thymic image obscuring both borders of the heart. Note scalloping of the left lobe of the thymus in contact with the anterior segment of the left fifth rib (arrow).

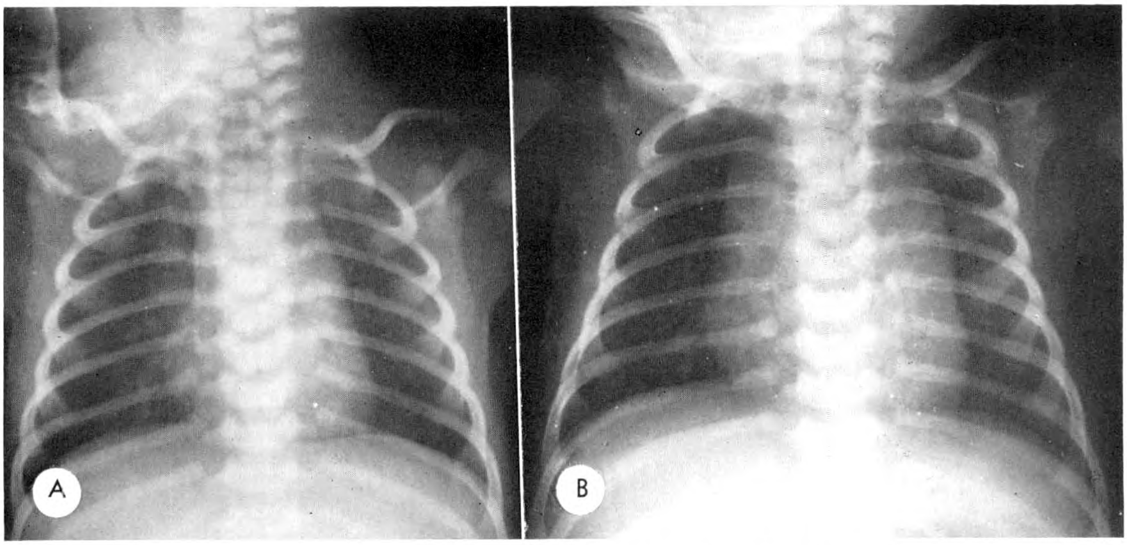

Fig. 6. Interval increase of thymic image during a 3 week period. (*A*) Thymic image at birth; (*B*) thymic image at the age of 3 weeks.

from a pneumothorax. This fissure line runs from the base of the lung on its lateral aspect to the horizontal fissure and will show pulmonary markings peripheral to it. Bulging intercostal spaces were encountered twice unilaterally (Fig. 10) and in one instance on both sides. These infants were clinically asymptomatic. There was one instance of suspicious pneumomediastinum in an asymptomatic infant. Three cases of pneumonia were found, including 1 case of massive aspiration of meconium and amniotic fluid. Neonatal atelectasis, confined to the right upper lobe, was noted in one case. A reticular pattern throughout both lungs, with diffuse small radiolucent images, was demonstrated in 1 case and suggested the possibility of hyaline membrane

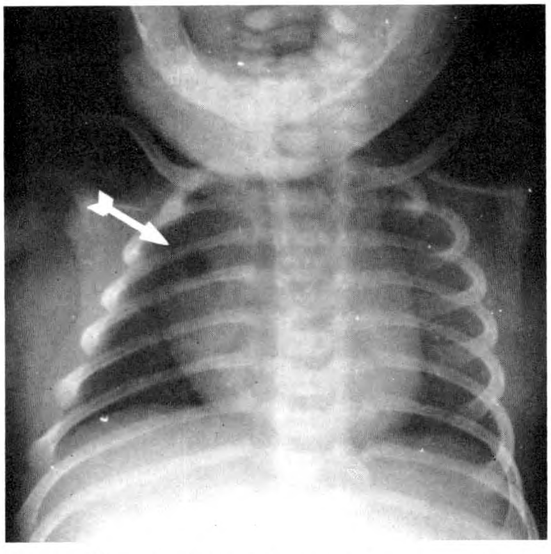

Fig. 7. Two radiolucent areas in a prominent right lobe of the thymus (arrow) presumed to represent fatty tissue in the thymus.

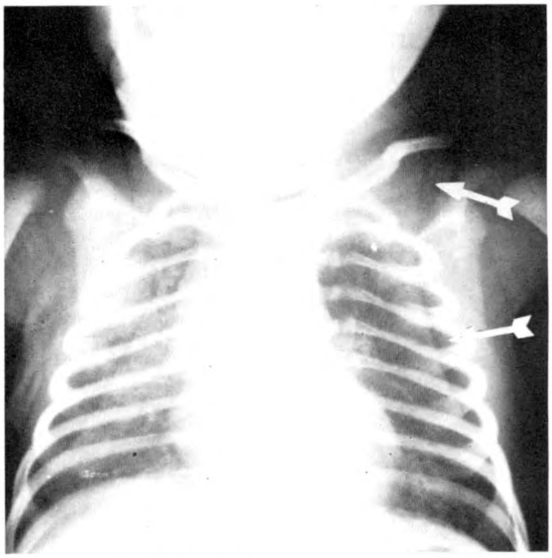

Fig. 8. Skin folds, which must not be mistaken for a pneumothorax (lower arrow). They frequently extend beyond the confines of the thorax, toward the neck or abdomen. Note extension into the neck (upper arrow).

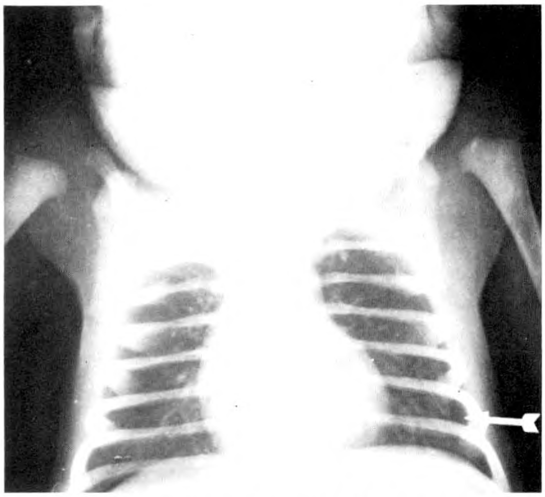

Fig. 9. Pneumothorax over the lateral aspect of the left lower hemithorax (arrow).

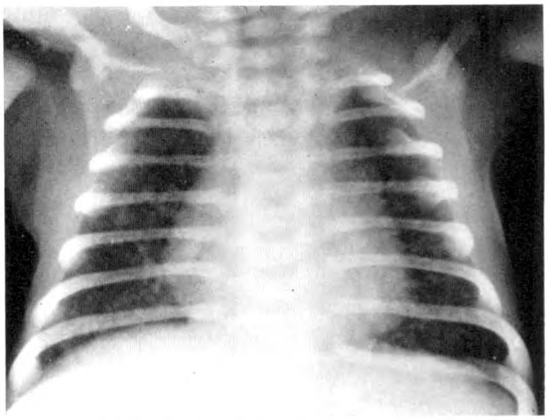

Fig. 11. Diffuse reticular pattern in both lungs, with small radiolucent images suggesting hyaline membrane disease, seen in an asymptomatic newborn; presumably representing a normal variant.

disease. This was not confirmed by the clinical record. The child was asymptomatic and we were presumably dealing with a normal variant in a newborn (Fig. 11). As pointed out above, an air bronchogram was noted intramediastinally on several occasions.

A right cardiophrenic density was visualized in 5 instances and was attributed to pericardial fat.

A unilateral radiolucent lung was demonstrated on the left side in one instance (Fig. 12). A follow-up examination on the second day of life showed normal aeration bilaterally. Retrospectively, in this asymptomatic infant, the unilateral hyperlucent lung on the left is attributed to rotation.

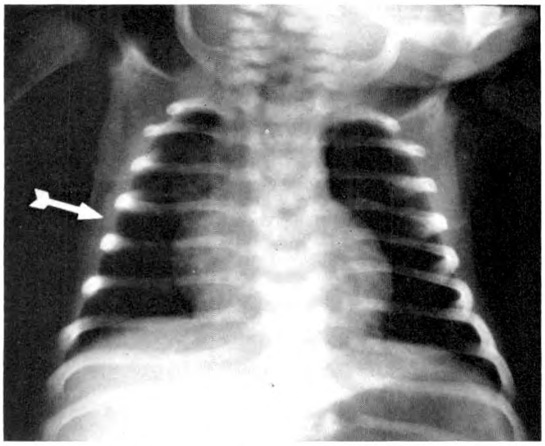

Fig. 10. Bulging intercostal spaces along the right lateral hemithorax (arrow). Although this sign may be encountered in the presence of obstructive emphysema, it frequently represents a normal variant.

ANOMALIES OF THE CARDIAC CONTOUR

A boot-shaped heart with elevation of the cardiac apex was seen in 4 instances (Fig. 13). A review of the patients' clinical

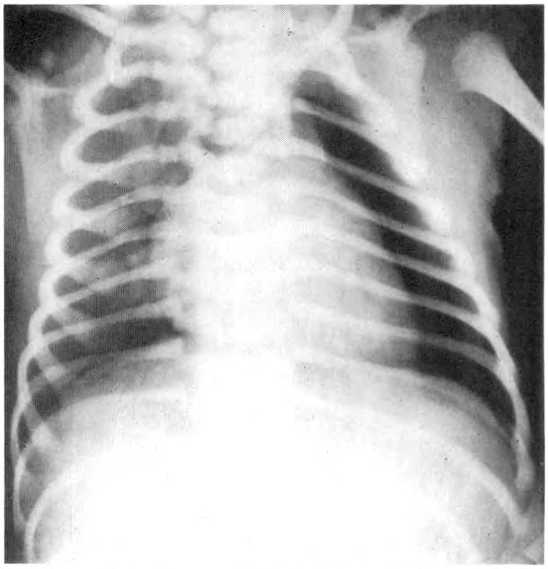

Fig. 12. Apparent unilateral left radiolucent lung attributed to rotation. Follow-up examination on the second day of life showed symmetric aeration of the lungs.

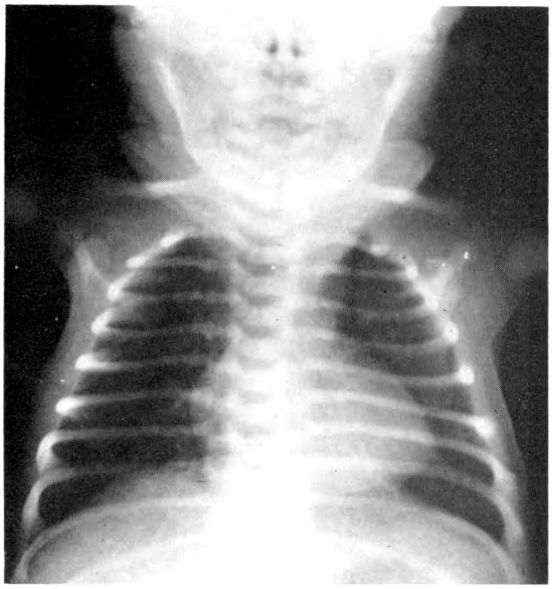

FIG. 13. Bizarre cardiac configuration with "boot-shaped" apex in an asymptomatic child whose physical examination was normal; presumably a normal variant.

records did not confirm any cardiac abnormality. A prominent left heart border was demonstrated in 3 instances, and a prominent right heart border in 2 instances. Prominence of the superior mediastinum, which was felt to be vascular in nature (because of its apparent extension above the thoracic inlet), was noted in 4 instances. (In one instance a left superior vena cava was strongly suggested on the roentgenogram.) As pointed out earlier in this report, no skeletal abnormalities were encountered.

SUMMARY

A series of 1,020 consecutive newborns was examined by means of frontal chest roentgenograms. Particular attention was directed to the patterns of thymic prominence. In about one-half of the cases, there was no prominence of the thymus on either side. In the remaining half, prominence of the thymus involved much more frequently the right lobe than the left. The various grades of thymic prominence on both sides are illustrated. The differential diagnosis of thymic prominence is discussed.

Incidental findings in the lung and cardiovascular system, including the frequency of visualization of the horizontal fissure, the presence of skin lines simulating a pneumothorax and other normal variants, are briefly described. No skeletal abnormalities were noted in this series.

The reported study shows that wide variations exist in the normal appearance of the newborn thorax. These should be taken into consideration by the interpreting radiologist.

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ABERRANT RIGHT SUBCLAVIAN ARTERY IN MONGOLISM*

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AN ABERRENT right subclavian artery is one which arises as the last branch of a left aortic arch instead of from the innominate artery. This anomaly is found in 0.5 to 1.3 per cent[1,2,6,13] of the normal population as reported in large autopsy series. An aberrant right subclavian artery was first described by Hunauld[9] in 1735 from autopsy findings and its roentgen features were first noted by Kommerell[10] in 1936.

The association of aberrant right subclavian artery and mongolism was originally reported by Strauss[14] in 1953. She noted the aberrant artery in 2 cases of mongolism at autopsy, one with and one without associated congenital heart disease. Since then, several other authors have reported an aberrant right subclavian artery in mongoloids, ranging in incidence from 1.6[7] to 4.5 per cent.[12] This association is not well known. In 2 recent monographs on mongolism,[3,8] an aberrant right subclavian artery is not mentioned; in another[5] only 1 case in 134 mongoloids is reported.

Because several mongoloids at The New York Hospital were recently noted to have this anomaly in a barium swallow cardiac series, further investigation of its incidence as seen on barium esophagrams seemed warranted.

MATERIAL AND METHODS

All cases of mongolism in children seen at The New York Hospital from 1949 to 1964 were reviewed. Of 114 mongoloids seen in this period, roentgenograms were located of 52. Barium esophagrams had been made in 28 of the 52, usually for cardiac evaluation. Twenty-seven of these 28 were found to have congenital heart disease.

Of more than 700 mongoloid patients at the Willowbrook State School in Staten Island, New York, 87 randomly selected ambulatory cases ranging in age from 8 to 47 years were examined by fluoroscopic spot roentgenograms in the frontal and lateral projections. The exact cardiac status of this group was unknown. Of those fluoroscoped, 75 had roentgenograms which were adequate for review.

To discover the incidence of aberrant right subclavian artery in children with known congenital heart disease who were not mongoloids, the roentgenograms of 131 children seen at The New York Hospital in 1964 by one pediatric cardiologist were reviewed. Of this group, 103 had adequate barium esophagrams.

ROENTGEN DIAGNOSIS

A characteristic roentgen appearance is usually seen with an aberrant right subclavian artery. In the frontal projection, there is a shallow oblique impression on the barium filled esophagus ascending from the level of the third or fourth thoracic vertebral body on the left to the level of the second or third vertebral body on the right (Fig. 1*A* and 2*A*). This vessel is occasionally seen on the plain posteroanterior chest roentgenogram. The lateral view shows a small caliber impression posterior in location (Fig. 1*B* and 2*B*). Beabout *et al.*[2] and Stewart *et al.*[13] reviewed thoroughly the many reports in which it was stated that the aberrant artery passes behind the esophagus in 80 per cent of cases, between the esophagus and trachea in 10–15 per cent and in front of the trachea in 10–15 per cent and concluded that passage of the vessel in front of the trachea or between the trachea and esophagus rarely if ever occurs.

The deformity on the esophagus is sometimes mimicked in the anteroposterior

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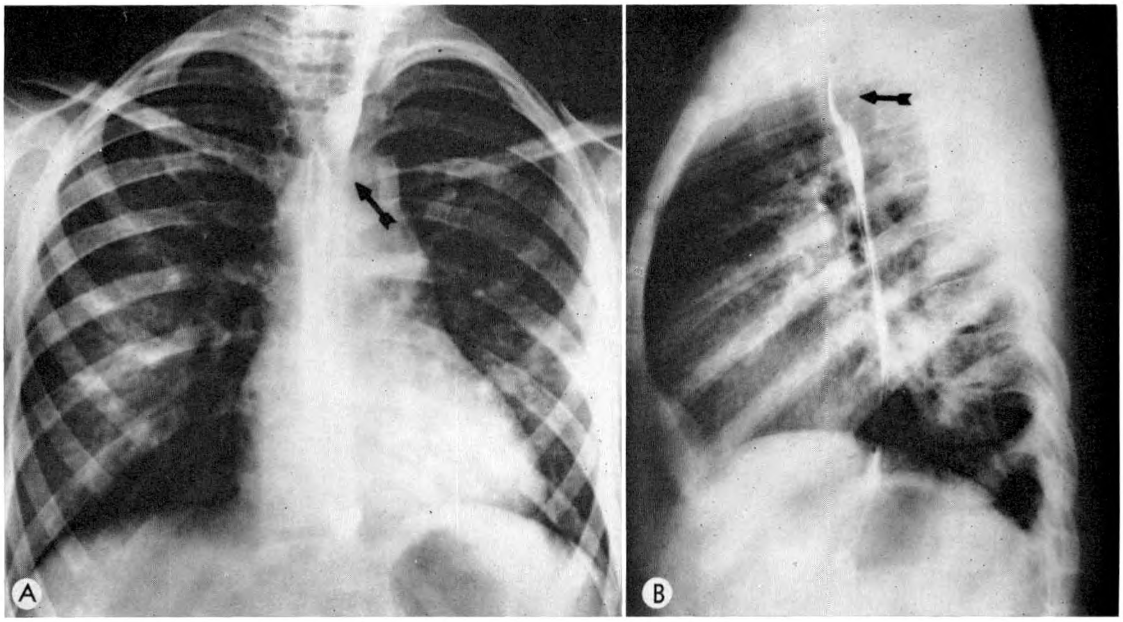

Fig. 1. Typical appearance of aberrant right subclavian artery as seen on the barium esophagram (*A*) Frontal study; (*B*) lateral study.

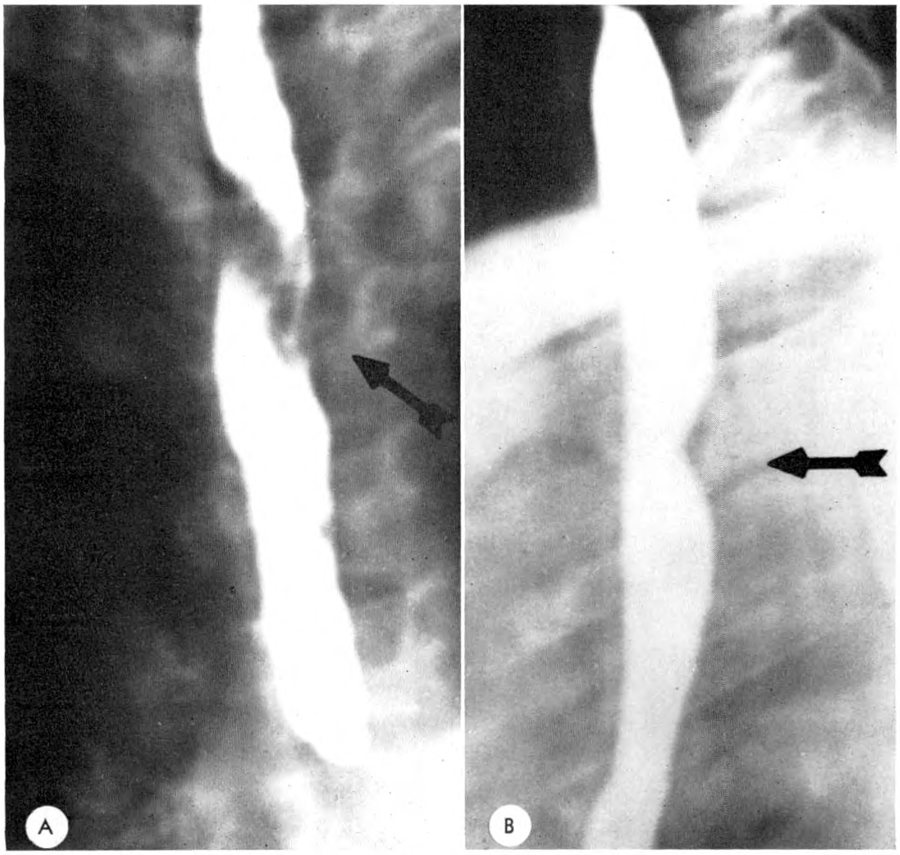

Fig. 2. Appearance of aberrant right subclavian artery on fluoroscopic spot roentgenograms with barium swallow. (*A*) Frontal projection; (*B*) lateral projection.

Table I

SUMMARY OF RESULTS FROM THE LITERATURE AND IN PRESENT SERIES

Mongoloid Cases	Total No. of Cases	No. with Congenital Heart Disease	No. with Barium Study	No. with Aberrant Right Subclavian Artery		Incidence of Aberrant Right Subclavian Artery	
				total	with congenital heart disease	total	with congenital heart disease
New York Hospital	28	27	28	10	10	35.7%	37%
Willowbrook State School	87	?	75	14	?	19%	?
Evans[7]—Autopsy Series	63	28	—	1	1	1.6%	3.6%
Strauss[14]—Autopsy Series	12	6	—	1	1	8.3%	16.6%
Rowe and Uchida[12]—Clinical and Autopsy Series*	157	65	142	7	2	4.5%	3.1%
Non-mongoloid Cases with Congenital Heart Disease at New York Hospital	131	131	103	0	0	0	0
Normal Population Autopsy Series						0.5–1.3%	

* Six patients were studied only at autopsy.

roentgenogram by pressure of the left main stem bronchus. This occurs at a lower level and is easily differentiated. Vascular rings causing a filling defect are usually much larger in size. An occasional aberrant vessel may not cause a filling defect. This may occur when the esophagus is not fully distended.

RESULTS

The results of the present study are summarized in Table 1. Of the 114 mongoloid children in The New York Hospital study, 28 had barium swallow cardiac series. Congenital heart disease was confirmed in 27. In 10 of the 28 (35.7 per cent), an aberrant right subclavian artery was found. None of the non-mongoloid children with congenital heart disease reviewed at The New York Hospital demonstrated this anomaly. In a series of older mongoloids (average age 19.5 years) examined at the Willowbrook State School, 14 of 75 (19 per cent) were found to have an aberrant right subclavian artery.

DISCUSSION AND SUMMARY

A high incidence of aberrant right subclavian artery was found in cases of mongolism. This was especially so in those with proven congenital heart disease. Most authors[3,4,11,12] agree that cardiac defects in mongoloids are much more commonly seen in younger than older subjects. The group of mongoloids seen at Willowbrook State School with an average age of 19.5 years showed a 19 per cent incidence of aberrant right subclavian artery. The incidence in the mongoloid children at The New York Hospital with congenital heart disease was 37 per cent. No aberrant right subclavian arteries were found in the non-mongoloid children with congenital heart disease at The New York Hospital.

It may be concluded that an aberrant right subclavian artery is found in a high proportion of mongoloids, and, when seen, should suggest the need for further cardiac evaluation.

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THE PALEOPATHOLOGIC RIDDLE OF "SYMMETRICAL OSTEOPOROSIS"*

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EXAMINATIONS of ancient remains recovered during the past century from archeologic excavations have revealed a large variety of congenital and acquired pathologic conditions in the skeletons of prehistoric peoples. The nature of some of these pathologic lesions has been obvious. In many instances, however, the pathogenesis of the osseous abnormalities has continued to be a matter of conjecture. Prominent among these puzzling bone defects is a frequently found abnormality of the skull which Hrdlička[7] called "symmetrical osteoporosis." This abnormality consists of a symmetrical coral or sieve-like porosity involving the outer surface of the skull or parts of it (Fig. 1 and 2). The diploic space is widened in the involved area. The outer table is absent or porous but the inner table is intact. When roentgenographed, the involved areas show widened diploic space and radial striation of bone spicules at right angles to the tables (Fig. 3 and 4). The roentgen appearance is that of the hair-on-end pattern seen today in several forms of anemia.

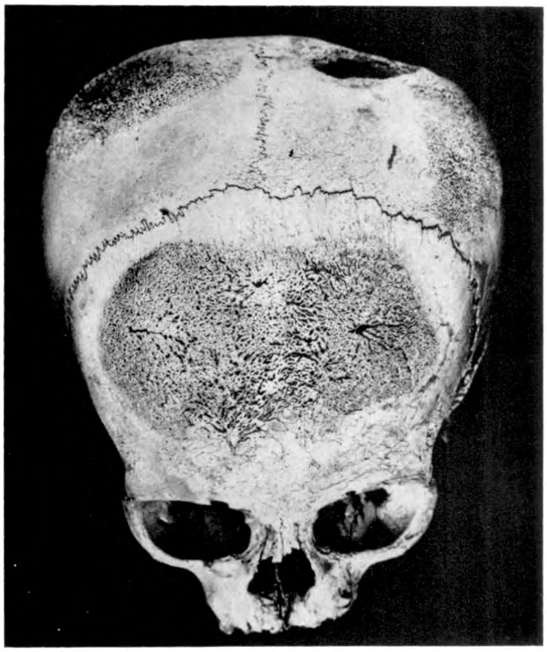

FIG. 1. Skull of pre-Columbian Peruvian Indian child showing "symmetrical osteoporosis" of the frontal and parietal bones. The skull is approximately 700 years old as determined by the radiocarbon dating method. There is a coral or sieve-like appearance of the involved areas. The surface of the skull is perforated by multiple small pores or empty columns which communicate with the diploic space. A segment has been removed from the left parietal bone for pathologic and roentgenologic study.

On expeditions to South America in 1910 and 1913 Alěs Hrdlička, the American physical anthropologist, found this condition to be frequent in the skulls of ancient pre-Columbian Peruvian Indians. He noted that skulls of this type were frequent among the skeletal remains found along the coastal regions of Peru but were absent in those from the mountains. Hrdlička,[7] a prodigious worker gifted with extraordinary powers of observation, description and the recording of detail, described this paleopathologic finding in 1913 in the following passage: "A peculiar disease, or a manifestation of a disease, occurring quite commonly in infancy among the prehistoric Peruvians of the coast. Found by the writer in 1910 at Pachacamac and Chicama and at all other parts of the coast that were examined in 1913. It was absent in the mountains and along the coast its frequency and perhaps its grade differed from locality to locality. This condition of the skull began to manifest itself in infancy or early childhood. The osseous changes were, so far as could be determined, limited to the cranium, all other parts of the skeleton remaining normal. In all probability they

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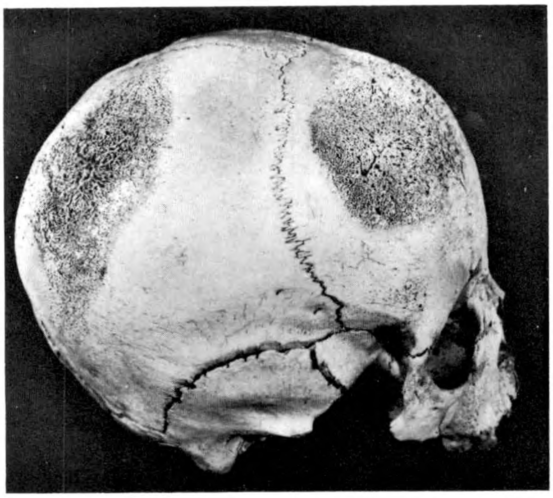

Fig. 2. Lateral view of same skull as in Figure 1 showing extent of lesions.

represented not a local disease, but an indication of some systemic disorder, and this was more likely of toxic than of nutritive or degenerative nature. The disorder was often fatal and that mostly before the changes in the skull reached their maximum; but in a fair percentage of cases the subject recovered. The changes on the skull were characterized by considerable symmetry, by limitation to a very large extent to the outer surface, by invasion of only those parts which do not give attachment to muscles and by the avoidance of the sutures as well as the facial portions, thus differing radically from such diffuse osteoporosis as described in apes by v. Hansemann. The process began, as can well be seen from the numerous specimens, in the roof of the orbits or on each side of the frontal squama, between the frontal tuberosity and the coronal suture. In the orbits it began by an increase of vascularity, followed by deposition of porous tissue, which in extreme cases came to look exactly like a low growth of coral. On the frontal the first changes were more like those of localized periostitis, but eventually led also to more or less surface osteoporosis. Following the frontal, more exclusively osteoporotic manifestations developed on the posterior portion of each parietal, between the temporal crest and the sagittal suture, and on the occipital above the crest. If the condition still advanced, then the wings of the sphenoid, parts of the temporals and parts of the base with the palate began to show signs of proliferation and fine osteoporosis, while localized breaking down of the altered tissue may have taken place in one or more of the older lesions. These were evidently the limits of the bone changes. If recovery took place there was some thickening of the affected parts of the skull, disappear-

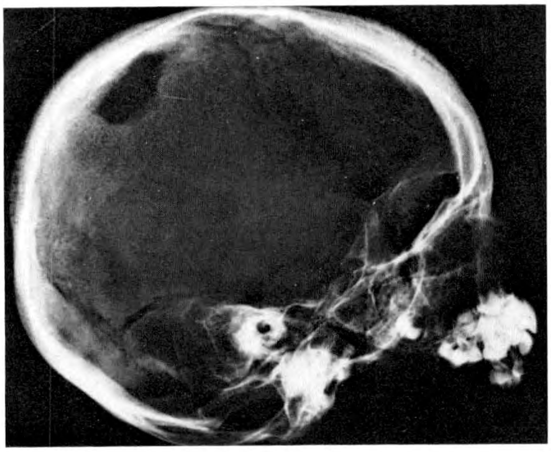

Fig. 3. Roentgenogram of same skull as in Figures 1 and 2 showing widening of the diploic space in the frontal and parietal areas. Spicules of bone are arranged perpendicular to the tables and extend outside the poorly defined outer table uncovered by a bony plate. There is no major involvement of the facial bones.

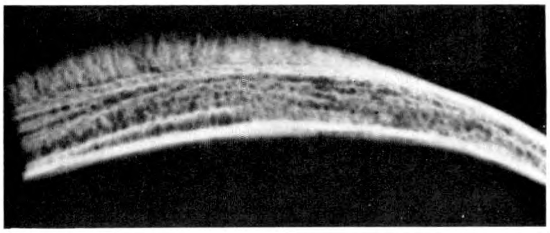

Fig. 4. Roentgenogram of segment taken from the left parietal bone. The diploic space is widened and contains a network of diploic trabeculae. The inner table is compact. The outer table in the involved portion is porous and external to it spicules of bone are arranged in a radial pattern perpendicular to the tables and are uncovered by a bony plate. The outer table in the uninvolved portion to the right of the section is thick and compact and the diploic space in this area is smaller.

ance of all overgrowths and a persistence of more or less of a sieve-like condition of the altered surfaces. The rest of the skeleton, as already stated, was either unaffected or affected but slightly."

Hooton,[6] the former distinguished physical anthropologist at Harvard, found the condition to be common in the skulls of immature subjects found in the Sacred Cenote of Chichen Itza in the Yucatan. In fact, in 21 well preserved skulls of children between the ages of about 6 and 12 years from that site, marked symmetrical osteoporosis was noted in no less than 14 or 66 per cent. From the skulls of older individuals recovered from the same sacred well, he claimed to be able to distinguish various less active phases of the condition, including some with almost completely healed lesions. Other reports[16,19] have described the finding of symmetrical osteoporosis in some skulls of pre-Columbian Indians of North America. These would indicate a greater frequency of the condition in the vicinity of New Mexico and Arizona but a few such skulls have been found in the northern part of the United States, including New York State. There are also reports which indicate that symmetrical osteoporosis has been present in ancient skulls found in Egypt, Europe and Indonesia.

Early attempts to explain the pathogenesis of these cranial abnormalities were severely handicapped by the limited knowledge of bone pathology available during that period, and causative factors such as rickets and syphilis were suggested by some, while others mentioned the possible influence of toxic or endocrine disorders. It was even suggested that the condition might have resulted from pressure due to the carrying of water jars on the head.

Williams' extensive report[19] on human paleopathology with observations on symmetrical osteoporosis appeared in 1929 and Hooton's description of the condition in Mayan and North American Indians was published in 1930.[6] By that time Cooley and his associates[2,3] had described what is now known as Cooley's anemia or thalassemia major, and Reynolds had described the skull changes in that condition.[3] In 1930, Vogt and Diamond[15] provided a more definitive exposition of the roentgen findings in congenital anemias. They reported 19 patients with severe anemia. Five of these had congenital hemolytic jaundice (hereditary spherocytosis); 13 were cases of erythroblastic (Cooley's) anemia and 1 had sickle cell anemia. The marked similarity of the skull changes in all 3 conditions was noted. When shown roentgenograms of ancient skulls from the Yucatan by Hooton, Edward Vogt, then roentgenologist to the Children's Hospital of Boston, suggested that the condition called "symmetrical osteoporosis" by the anthropologists indeed appeared identical to the skull changes which were then being found in the congenital hemolytic anemias. Very little, however, has been added to the solution of this perplexing problem since then and there is a general feeling among those who come in contact with the problem that these prehistoric people suffered from a hemolytic anemia, most likely thalassemia.

Advances in hematology and radiology during the past decade make it possible to re-examine this problem with some new insights. The number of hemolytic processes which we now know are capable of producing a hair-on-end pattern of bone change in the skull, for instance, has increased and some nonhemolytic conditions have been found to produce similar changes. Thus, in addition to thalassemia major (Fig. 5), sickle cell anemia and hereditary spherocytosis, the pattern of symmetrical osteoporosis may be found in the skulls of patients with thalassemia minor, hereditary elliptocytosis, nonspherocytic hemolytic anemia due to red blood cell enzyme deficiencies (Fig. 6), iron deficiency anemia (Fig. 7), polycythemia and cyanotic congenital heart disease. Table 1 is a partial list of conditions which may produce such cranial lesions. The pathologic common denominator of these disorders is erythroid hyperplasia of the bone marrow

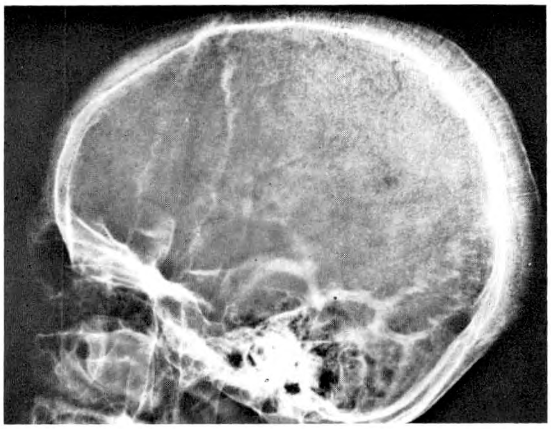

Fig. 5. Cooley's anemia. The skull shows a hair-on-end pattern involving the parietal and upper occipital bones. While the diploic space is widened in the frontal bone, the outer table is compact and intact and there is no radial spiculation of bone. In the parietal bone the diploic space is widened but the outer table is porous and fragmented where hyperplastic marrow has perforated it and proliferated subperiosteally. In this area spicules of bone have arranged themselves perpendicular to the tables. In the occipital area the hyperplastic marrow has almost completely destroyed the outer table. The maxillary sinuses are incompletely aerated.

in infancy or childhood. The hyperplastic cellular marrow between the tables of the skull widens the diploic space and thins the outer table. The partially atrophied outer table is then perforated by the expanding marrow which proliferates subperiosteally. In time, the outer table may be completely destroyed. Stimulation of the periosteum produces new bone which eventually is calcified and is arranged parallel to marrow vessels which are perpendicular to the inner table.[4,11] At this advanced stage the columns of hyperplastic marrow open onto the surface of the skull under the periosteum but are uncovered by a bony plate. D'Eramo and DeGaetano[4] contend that in some instances hyperplastic marrow may also extend through the inner table and produce a hyperostosis which differs from the pericranial new bone spiculation since it is kept more compact by intracranial pressure. The anthropological term "symmetrical osteoporosis" coined by Hrdlička is really unsuitable for this process and the condition has been more aptly called spongy hyperostosis of the cranium. Hamperl and Weiss[5] have emphasized the desirability of this latter designation. Investigators dealing with this spongy hyperostosis of prehistoric crania have described and discussed the skull in detail, but comments regarding abnormalities of the remaining skeleton have been either lacking or too general to aid in diagnosis. The appearance of the calvarium alone, however, does not provide any sound criteria for differential diagnosis, as in all cases the pattern of bone change is similar and is the result of erythroid hyperplasia of the marrow regardless of the mechanism of stimulation. Certain differences do exist in the reactions or lack of them of other parts of the skeleton to various hematologic processes. In Cooley's anemia one would expect a high incidence of inhibition of pneumatization of the maxillary sinuses due to expansion of the maxillary bone by hyperplastic marrow. Facial bone involvement in this erythroblastic anemia is the rule. On the other hand significant facial bone and sinus involvement would not be

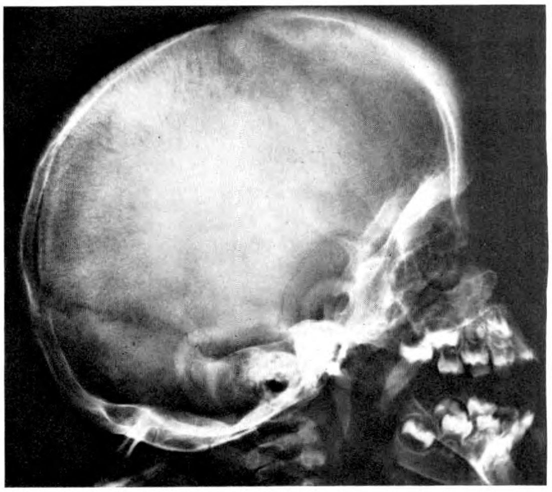

Fig. 6. Hereditary nonspherocytic hemolytic anemia of the pyruvate kinase deficient type. Skull of 2 year old white female shows thickening in the frontal region with radial striation of very fine spicules. The outer table is atrophied. In the parietal area there is coarser spiculation with typical hair-on-end appearance.

expected with any frequency in sickle cell anemia, thalassemia minor or iron deficiency anemia. In children, advanced hyperplastic marrow changes in the central and appendicular skeleton would usually be seen in Cooley's anemia but would be mild or frequently absent in most children with sickle cell disease, even milder in thalassemia minor and probably absent in iron deficiency anemia. If such skulls were the result of sickle cell anemia or its genetic variants, some long bones should be found among the older children or adults which would show evidence of infarctions or cortical thickenings. If the skull changes were due to thalassemia minor, then skeletons showing changes consistent with thalassemia major should also be found among the remains.

Hrdlička, describing the remains of ancient Peruvian Indians, maintained that the osseous changes were, so far as could be determined, limited to the cranium; all other parts of the skeleton remaining normal or being only slightly affected. He was of the impression that the pathologic process avoided the facial bones. Hooton, discussing the remains of pre-Columbian Mayan Indians in the Yucatan and several Pecos skeletons, confessed that he was never able to satisfy himself that bones other than those of the skull were affected. On the other hand, Williams[19] and Wakefield *et al.*[16] did describe some North American skeletons which were said to have some long bone alterations. The meager descriptions of these suggest that they may have been the sites of hyperplastic marrow with thinning of the cortices. The need for further study, especially roentgenographic examination of skeletons in which the skulls have shown symmetrical osteoporosis, seems clear. At least, the presence of the major hemolytic disorders, thalassemia major and sickle cell disease might be confirmed or excluded.

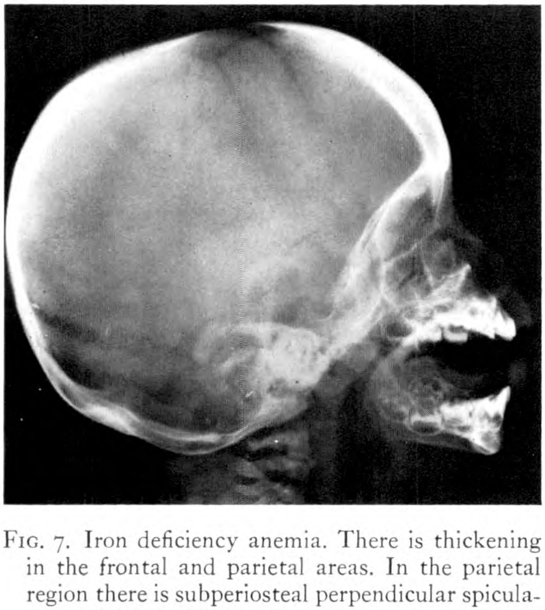

Fig. 7. Iron deficiency anemia. There is thickening in the frontal and parietal areas. In the parietal region there is subperiosteal perpendicular spiculation of bone. The patient is a 10 month old Puerto Rican boy born to an anemic mother. He was fed a diet almost exclusively of milk with some vitamin supplements. The remaining skeleton showed no abnormalities.

Table I

Incomplete List of Conditions Which May Cause a Hair-on-End Pattern in Skull

I. *Congenital Hemolytic Anemias*
  - Thalassemias
    - Thalassemia major—Cooley's anemia
    - Thalassemia intermedia
    - Thalassemia minor
    - Thalassemia—hemoglobin S disease
    - Thalassemia—Lepore hemoglobin disease
    - Thalassemia—hemoglobin E disease
  - Sickle Cell Disease
    - Sickle cell anemia
    - Sickle cell—hemoglobin C disease
    - Sickle cell—thalassemia
  - Hereditary Spherocytosis (Spherocytic anemia)
  - Hereditary Elliptocytosis
  - Hereditary NonSpherocytic Hemolytic Anemia
    - Pyruvate kinase deficiency
    - Probably others

II. *Iron Deficiency Anemia*

III. *Cyanotic Congenital Heart Disease*

IV. *Polycythemia Vera in Childhood*

Hereditary spherocytosis could be the cause of changes similar to those of symmetrical osteoporosis, but, even in the untreated state, this condition is usually prolonged and relatively benign and the finding of frequent involvement of the bones of

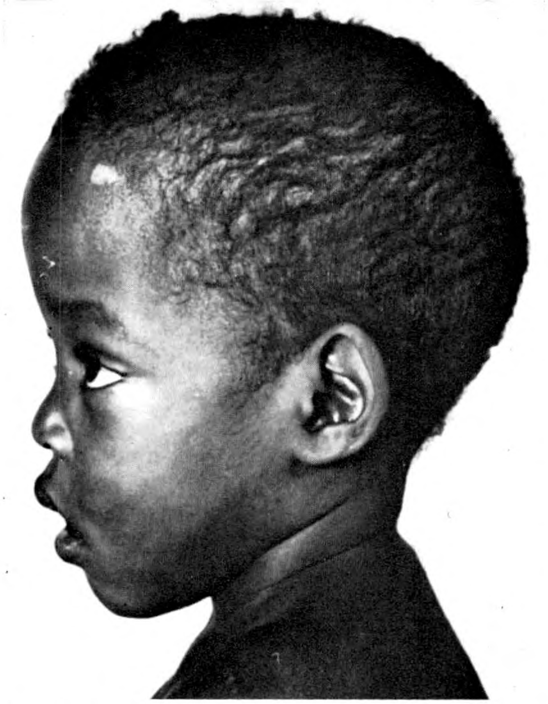

Fig. 8. Bahima disease. Young child of the "Hamitic" Bahima people of Uganda. The skull is high and frontally bossed. In the frontal and fronto-temporal regions there are rounded scars from indigenous therapy by branding.

infants and young children would seem unlikely, at least, in the evolution of the disease as we see it today.

Hereditary elliptocytosis, as currently seen, is generally a very benign disorder which only rarely causes hemolytic anemia, and, while cases with skull changes have been described, they are rare indeed. The incidence of this condition has not yet been determined.

The nonspherocytic hemolytic anemias due to enzyme deficiencies, especially pyruvate kinase deficiency, are capable of producing similar skull changes but we have not had the opportunity to study the appendicular skeleton in any of these cases to date. The incidence of these hemolytic disorders is yet to be firmly established.

In the past 8 years, it has been well documented that iron deficiency anemia in infants and children can result in skull changes identical to those occurring in the congenital hemolytic anemias.[1,10,12,13] Such cases have been described in many different parts of the world (Indonesia, Mexico, Europe and the United States) and in several different races. Significant involvement of bone in iron deficiency anemia appears to be limited to the skull. Most of these young patients have suffered from poor diets which consisted mainly of milk. Some cases have been reported, however, in which the anemia was due to chronic blood loss. Lie-Injo[10] has described a 12 year old girl with such skull changes, for instance, whose anemia was secondary to chronic blood loss from the intestinal tract due to hookworm infestation.

In this connection in a recent interesting report, Jelliffe and Blackman[9] describe a condition occurring among the children of the "Hamitic" Bahima people of Uganda. These children present with slightly tower-shaped, sometimes bossed, skulls which are recognized by parents in early life and treated by multiple branding (Fig. 8). Roentgenologic examination of these skulls shows diploic widening and hair-on-end spiculation identical to that seen in the hemolytic anemias (Fig. 9), but there is no evidence of thalassemia, sickle cell disease or other hemolytic process. All of the children examined showed some degree of iron deficiency anemia. The Bahima people are a pastoral group in whose culture cattle occupy a dominant position. Milk in various forms is the major nutritional item of the diet and is fed to infants from the early months of life in as large quantities as possible. Other foods play a minor or even negligible role. Milk is the cultural "superfood" for young and old alike and is traditionally considered all that is necessary for children. Jelliffe and Blackman have suggested that this widespread cranial abnormality, which is referred to in Uganda as "Bahima disease," is due to chronic iron deficiency anemia resulting from a diet almost exclusively of milk. This is the first report suggesting such frequent involvement of the skull from iron deficiency anemia directly related to the cultural environment, and it would tend to strengthen the possibility that symmetrical osteoporosis seen so frequently in the ancient skulls of Peru and the Yucatan may, in fact, be the result of iron deficiency anemia.

It does not seem necessary, of course, to ascribe the same etiology to all skulls with symmetrical osteoporosis, at least, not to those found in widely different areas, but the current, although rather vague, impression that the condition is a manifestation of paleontologic thalassemia[20] does not appear to be well supported by the facts. In addition to Hrdlička's and Hooton's contention that there was no significant involvement of the facial or long bones in the Peruvian and Yucatan skeletons, thalassemia does not exist in the Peruvian Indians of today,[14] nor has sickle cell disease been recorded in those Indians who are unmixed.

The application of modern radiographic techniques to the study of other portions of these ancient skeletons should provide data of more diagnostic value. Such findings when considered in the light of our current knowledge regarding gene distribution, mutation and polymorphism and our knowledge of ancient dietary habits can provide a step forward in the solution of this paleopathologic riddle.

It is surprising that even today the scope of radiologic investigation is largely neglected by archeologists. The value of such examinations in the detection of pathology not apparent on gross inspection of a bone hardly needs to be stressed to anyone vaguely familiar with diagnostic roentgenology. Radiography is also one of the most useful means of examining mummies.[17] When these are found in cartonnage packs or wrapped in friable bandages, radiography may be the only way in which they can be examined. Wells[18] has recently introduced radiography in archeology as a means of comparing morbidity rates between ancient populations. This is done by observing the number of growth arrest lines in the long bones of a sample of individuals from various locations.

At a recent symposium on human paleopathology, Jarcho[8] called for a renewed interest and effort in this relatively dormant field by American scientists. The radiologist can and should play an important part in this expected resurgence.

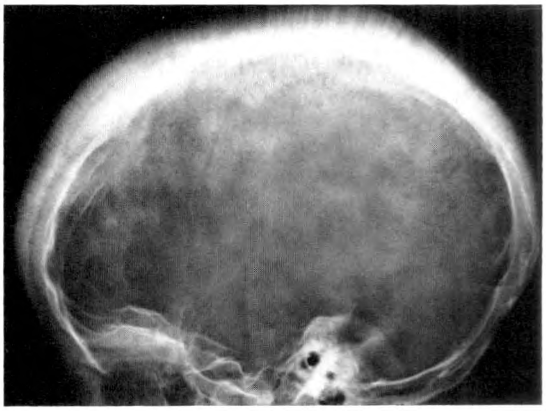

Fig. 9. Bahima disease. Skull of patient shown in Figure 8. There is widespread involvement of frontal and parietal bones with widening of the diploic space, coarse spiculation and dissolution of the outer table.

SUMMARY

A frequent finding in the skulls of prehistoric peoples, called "symmetrical osteoporosis" by the anthropologists, has been described and illustrated. Possible explanations for these bone alterations are reconsidered in the light of present hematologic and radiologic knowledge, and the need for fuller use of radiographic techniques in the investigation of this and other paleopathologic problems is discussed.

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THE SKULL ROENTGENOGRAM IN IRON DEFICIENCY ANEMIA AND IN SECONDARY POLYCYTHEMIA*

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THALASSEMIA and its variants, sickle cell anemia and related hemoglobinopathies, and congenital hemolytic jaundice are well known causes of abnormalities in the skull roentgenogram. Only recently has it been mentioned in the literature that similar skull changes may on occasion be produced by chronic iron deficiency anemia and by the secondary polycythemia of cyanotic congenital heart disease. The roentgenographic findings of the latter two entities are stressed in this report since they have received such little attention. Brief consideration is given to the pathology and underlying pathogenesis.

REPORT OF CASES

IRON DEFICIENCY ANEMIA

Case I. This 17 month old white male was admitted to the hospital because of pneumonia and failure to thrive. Physical examination revealed a poorly developed, poorly nourished child with pale yellowish skin and pallor of the mucous membrane. Except for a few scattered wheezes in the chest, the physical examination was within normal limits.

Laboratory studies revealed a hemoglobin of 3 gm. per 100 cc. and a hematocrit of 13 per cent. The red blood cells were microcytic and hypochromic with marked variation in shape; a bone marrow examination was compatible with the diagnosis of iron deficiency anemia.

After admission, the patient was treated with oral iron and improved markedly. He was asymptomatic at the time of discharge; the reticulocyte count was 3.1 per cent. Three months later, the hematocrit was 39.5 per cent and the hemoglobin was 14 gm. per 100 cc.

Skull roentgenograms showed a marked thickening of the calvarium, especially in the frontal area with thinning of the inner and outer tables. Distinct vertical striations were present (Fig. 1, 2 and 3).

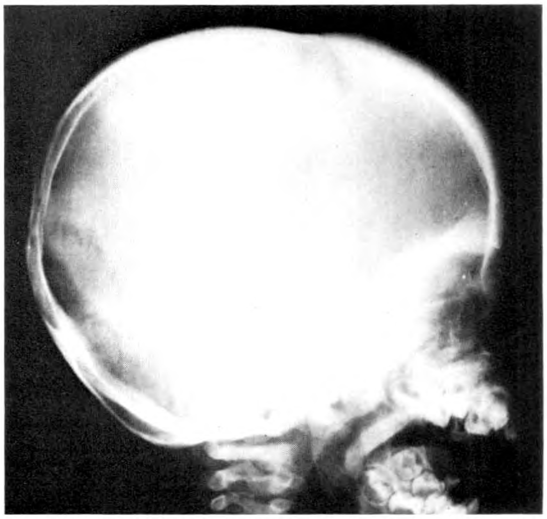

Fig. 1. Case I. Seventeen month old male with marked nutritional iron deficiency anemia. A lateral roentgenogram of the skull shows thickening of the diploë with thinning of the inner and outer tables of the calvarium, most marked in the frontal area.

SECONDARY POLYCYTHEMIA

Case II. This 2 year old white male was noted to be cyanotic shortly after birth. On physical examination a Grade III high-pitched systolic murmur, maximal in the second and third left intercostal spaces was heard; there were no diastolic murmurs. A venous angiocardiographic study demonstrated transposition of the great vessels with a normal aortic arch and a large right-to-left shunt at the ventricular level.

The patient was hospitalized for most of the first year of life because of dyspnea, seizures, severe cyanosis and marked secondary polycythemia. The hematocrit ranged from 76 to

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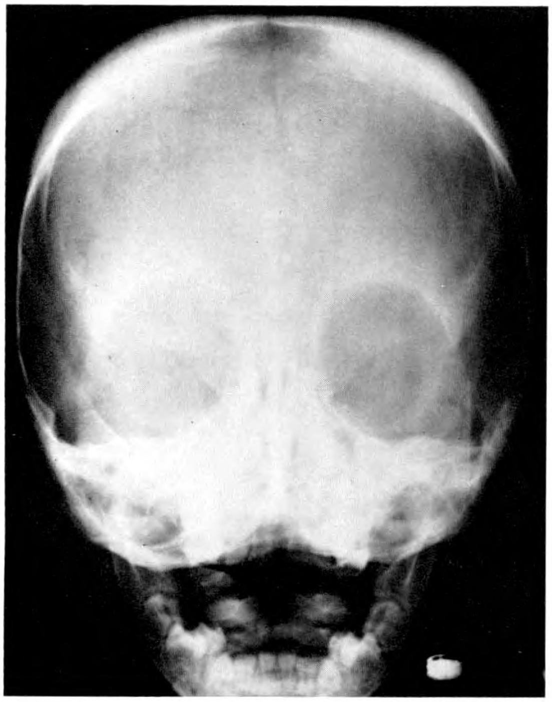

FIG. 2. Case I. Anterior roentgenogram shows the same finding in the frontal bone.

89 per cent with hemoglobin levels as high as 24.1 gm. per 100 cc.

The skull roentgenograms at the age of 21 months (Fig. 4, 5 and 6) showed marked thickening of the frontal bone and corresponding thinning of the inner and outer tables. On a close-up study coarse vertical striations were noted. The spine and peripheral bones were roentgenographically normal.

CASE III. This 3 year old white female was noted to be cyanotic shortly after birth. At cardiac catheterization, a complex lesion was demonstrated which included tricuspid atresia, a right-to-left shunt at the atrial level, a left-to-right shunt at the ventricular level and atresia of the ascending aorta. The systemic circulation was maintained by reversed flow through a patent ductus arteriosus. The hematocrit was 89 per cent with a hemoglobin level of 25.2 gm. per 100 cc. Roentgenograms of the skull revealed thickening of the frontal bone with corresponding thinning of the inner and outer tables. Because of the similarity to Case II, these roentgenograms are not reproduced here.

REVIEW OF THE LITERATURE

THALASSEMIA

Cooley's anemia or thalassemia forms a prototype for the anemias discussed in this paper and, therefore, is briefly considered. One of the major morphologic alterations of thalassemia occurs in the bone marrow which is markedly hyperplastic with an increase in the volume of active red marrow.[12] These pathologic changes form the underlying anatomic basis for the observed skull changes in thalassemia; similar, but generally less severe, pathologic alterations occur in all of the anemias de-

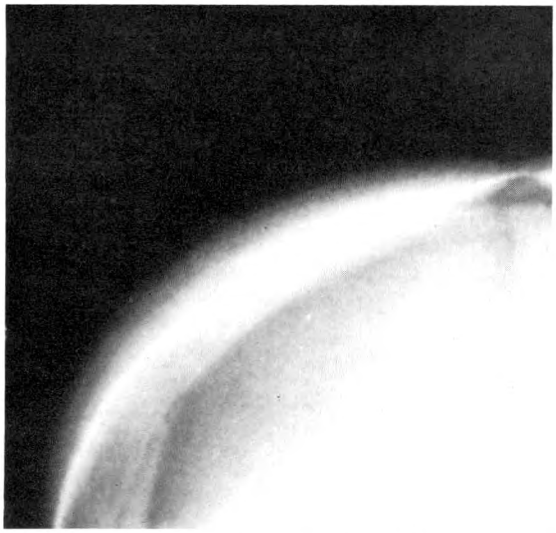

FIG. 3. Case I. A close-up tangential roentgenogram demonstrates fine vertical striations in addition to the thickened diploë.

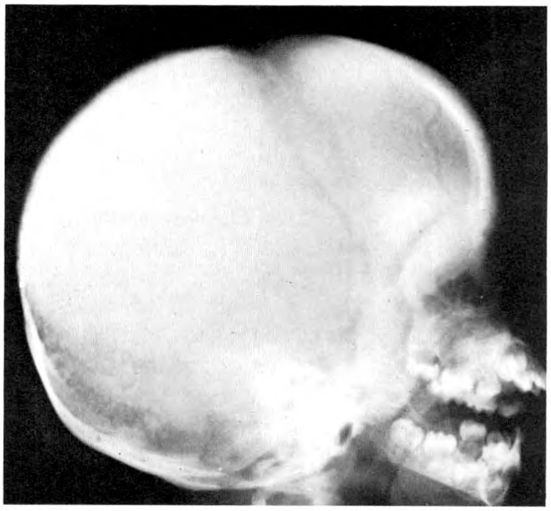

FIG. 4. Case II. A lateral roentgenogram shows thickening of the diploë with thinning of the tables, most marked in the frontal bone.

scribed herein. One should be aware that nutritional and metabolic factors also contribute to the pathology of the bone changes in the more profound anemias.

In a given patient with thalassemia, the bone changes are variable, depending upon the severity of the disease process, and may consist of any combination of the following roentgenographic findings:

1. Thickening of the cranial bones with the frontal bone being most prominently involved and the occipital squamosa below the internal occipital protuberance usually being spared.
2. Thinning of the inner and outer tables of the skull.
3. Widening of the diploic space, producing a so-called "hair-standing-on-end" appearance.
4. Diminished pneumatization of the paranasal bones, especially the maxillary antra. This abnormality is usually not encountered in the other anemias.
5. Hypertrophy of the upper maxilla.

Peripheral bone abnormalities are most marked in infants and tend to diminish in severity as the child grows older.[5] These changes are usually more prominent than in the other chronic hemolytic anemias. There is minimal spine involvement, predominantly enlargement of the medullary cavities. The severe cupping deformity and osteoporosis common in sickle cell disease are not usual features of thalassemia.

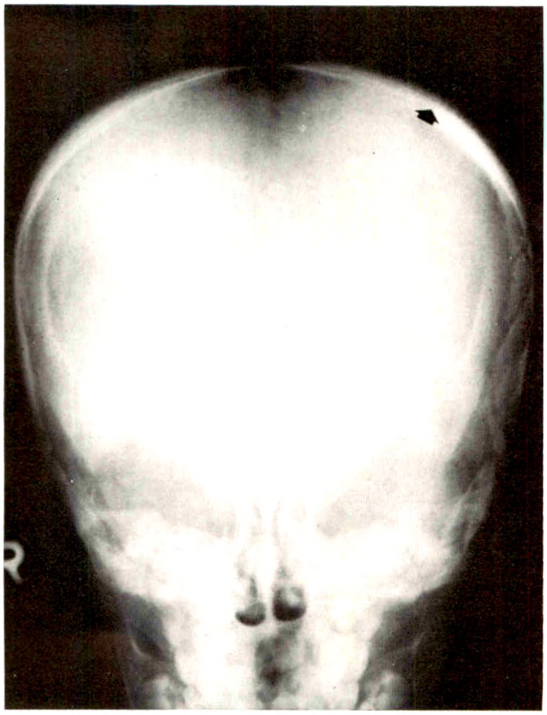

Fig. 5. Case ii. A frontal roentgenogram reveals distinct vertical striations (arrow).

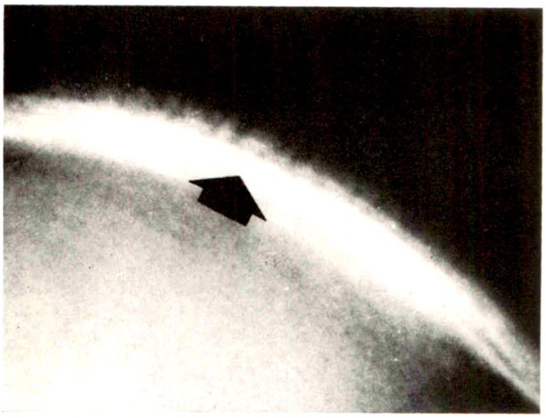

Fig. 6. Case ii. A close-up tangential roentgenogram shows the coarse vertical striations in addition to the thickened diploë.

SICKLE CELL DISEASE

Sickle cell disease and its variants may produce skull changes similar to those of thalassemia, but usually the findings are not as extensive.[10] However, in a given case, these two diseases often cannot be distinguished from skull roentgenograms alone, although markedly diminished pneumatization of the maxillary antra or other paranasal bones renders fairly certain the diagnosis of Cooley's anemia. On the other hand, the clinical picture, the hematologic features and peripheral bone roentgenograms usually make the differential diagnosis easy. The gross pathology of the bone marrow in sickle cell disease is similar to that of thalassemia.

CONGENITAL SPHEROCYTOSIS

Patients with hereditary spherocytosis or congenital hemolytic anemia may, on occasion, have skull roentgenograms similar to those seen in patients with sickle cell disease or thalassemia. The abnormalities are usually less severe and occur less frequently than in the patients with the other two diseases.

IRON DEFICIENCY ANEMIA

The roentgenographic skull changes of chronic iron deficiency anemia were first described in 1958 in a 12 year old Indonesian girl with a hemoglobin of 4.3 gm. per 100 cc.[7] Since that time several similar reports have appeared in the literature, some being cases of children born prematurely.[2,8,9,13] No changes have been observed in the peripheral bones, a finding in marked contradistinction to the congenital hemolytic anemias.

The usual alterations in iron deficiency anemia consist of widening of the frontal bones with thickening of the inner and outer tables and, at times, vertical striations. There has been no facial bone involvement in the reported cases. The roentgenographic skull changes are both unreliable and unpredictable as an index of the severity of the anemia.[8] Figures 1, 2 and 3 demonstrate these typical skull findings in our Case I.

POLYCYTHEMIA

Only recently has it been recognized that secondary polycythemia may cause abnormal skull roentgenograms. In 1940, Dykstra and Halbertsma[6] described thickening of the skull in the frontal area in an autopsy report of primary polycythemia in a 12 year old child, but no roentgenograms were available. Caffey[4] briefly mentioned that the secondary polycythemia of cyanotic congenital heart disease may produce abnormal skull changes, but did not comment further. In 1958, Ascenzi and Marinozzi[1] described in detail the roentgenographic skull changes of secondary polycythemia in 2 cases of tetralogy of Fallot. The first was a 3½ year old child whose skull roentgenograms showed a trabecular pattern with distinct striations; the second was a 6 year old child with a hematocrit of 88 per cent whose cranial bones showed parietal bossing, thinning and disappearance of the outer table as well as thinning of the inner table. Recently, 6 cases of roentgenographic peripheral bone abnormalities, secondary to the polycythemia of cyanotic congenital heart disease, have been reported; several of these patients had skull abnormalities as well as long bone changes.[11] The peripheral bone changes consisted of cortical defects, widening of the medullary canals, loss of diaphyseal tapering, and loss of trabeculation in some areas with coarsening in others. Figures 4, 5 and 6 show these abnormalities in the skull roentgenograms of Case II.

CLINICAL DATA AND DISCUSSION

Skull and peripheral bone roentgenograms were obtained of 24 additional cyanotic patients followed at the Grady Memorial Hospital Cardiac Clinic in an attempt to assess the incidence of skull changes in patients with cyanotic congenital heart disease and secondary polycythemia.

The diagnoses of these patients included: tetralogy of Fallot—14 cases; transposition of the great vessels—3 cases; transposition of the great vessels with tricuspid atresia—2 cases; atrioventricular canal with pulmonic stenosis—2 cases; pseudotruncus—1 case; dextrocardia, corrected transposition of the great vessels and pulmonic stenosis—1 case; and dextrocardia with undiagnosed cyanotic congenital heart disease—1 case. The average patient was 11.8 years old with an age range of 8 weeks to 43 years. Hemoglobin levels varied from 10 to 22.5 gm. per 100 cc. The hematocrit varied from 36 to 75 per cent with an average of 53.7 per cent. Arterial oxygen saturation levels were available for 14 of these patients and varied from 30.2 to 93.0 per cent, with an average of 73.8 per cent.

No further cases with abnormalities of the skull or peripheral bone roentgenograms were found; however, in none of the above patients was the secondary polycythemia as severe as in the 2 reported cases. The occurrence of roentgenographic skull changes is apparently dependent upon the severity of the polycythemia and correlates fairly well with the hemoglobin and hematocrit levels.

The pathology of the skull changes has recently been described by Mariani and Bosman.[8] In their study, the calvarium of 18 patients with cyanotic congenital heart disease was examined at autopsy. In 3 of these patients there was an increase of the diploë at the expense of the outer and inner tables, particularly the outer table. Occasionally, the marrow extended outward under the periosteum; none of the 3 cases had the trabecular rearrangement associated with striations.

The anemias described above and secondary polycythemia appear to have in common a hyperplasia or expansion of the bone marrow with the resultant changes in the skull, best detected on skull roentgenograms. The skulls of infants and children seem most susceptible to the effects of the expanding bone marrow.

SUMMARY

1. Several hematologic diseases may cause similar roentgenographic abnormalities of the skull. In this report the changes in chronic iron deficiency anemia and secondary polycythemia are stressed.

2. Roentgenographic skull changes produced by secondary polycythemia are uncommon and are probably related to the severity of the cyanosis and the degree of secondary polycythemia.

3. The exact mechanism of production of these bone changes is uncertain, but appears to be related to bone marrow hyperplasia.

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ANTERIOR FONTANEL BONES*

By BERTRAM R. GIRDANY, M.D., *and* EUGENE BLANK, M.D.
PITTSBURGH, PENNSYLVANIA

ALTHOUGH only 5 examples[1,2,3] of bones in the anterior fontanel have been recorded in literature, these intrafontanel bones are not rare. Thirty-one examples have been identified at the Children's Hospital of Pittsburgh. In 3 other children, accessory bones were located in the metopic sutures anterior to the fontanel. In one other child, wormian bones lay in the coronal sutures adjacent to the fontanel. The clinical significance and the growth patterns of these intrafontanel and intrasutural bones form the contents of this paper.

MATERIAL AND DISCUSSION

Thirty-one of the 35 children were boys. All the children were from different families; their siblings were not studied. In the 16 instances in which race was known, 15 children were white and 1 child was Negro. The parental ages of 7 children were known; the average maternal age was 28 years and the average paternal age was 31 years. Six boys were examined because of trauma. In at least 6 children, the bones in the anterior fontanels were palpated and the question of either too early closure or unusually small size of the anterior fontanel provided the indication for roentgen examination of the skull. The skulls of the other children were examined roentgenographically for a variety of reasons, including congenital defects, tumors, meningitis, and convulsions. It is probable that other examples of anterior fontanel bones were overlooked, and that some, although recognized, were not filed so as to be available for this report.

Anterior fontanel bones may be present at birth or may appear later. Single bones filled the anterior fontanels of 24 children. They were demonstrated in 5 children under 1 month of age (Fig. 1, *A* and *B*).

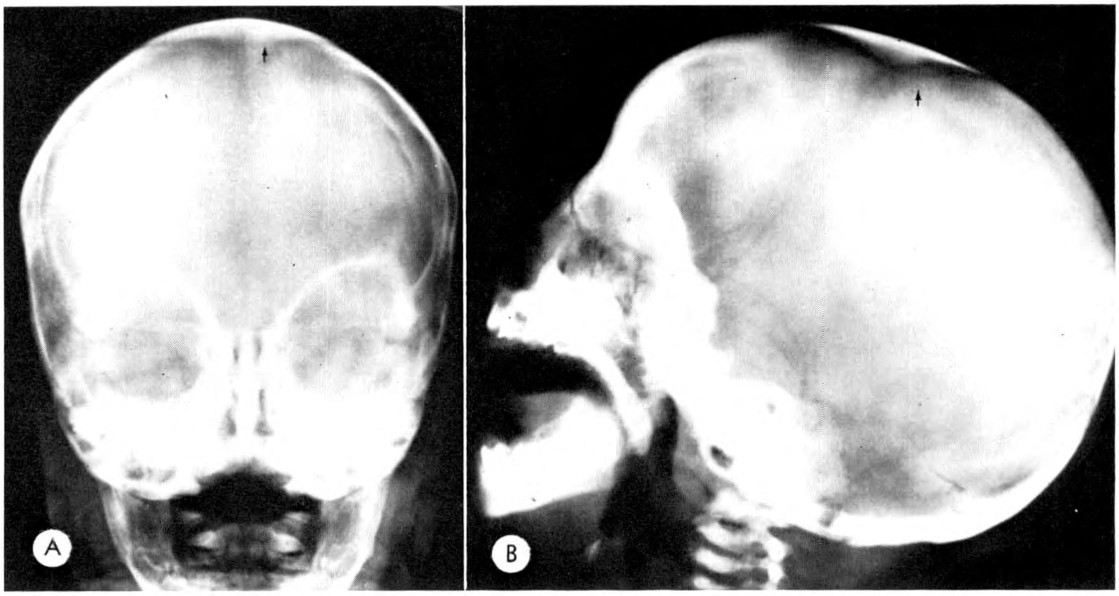

Fig. 1. (*A*) Frontal and (*B*) lateral projections. A large bone (↑) fills the anterior fontanel of a boy, 1 month of age. Its curve fits the curve of the skull. Normal growth of the skull occurred subsequent to this study.

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* From the Department of Radiology, Children's Hospital of Pittsburgh and the University of Pittsburgh, School of Medicine.

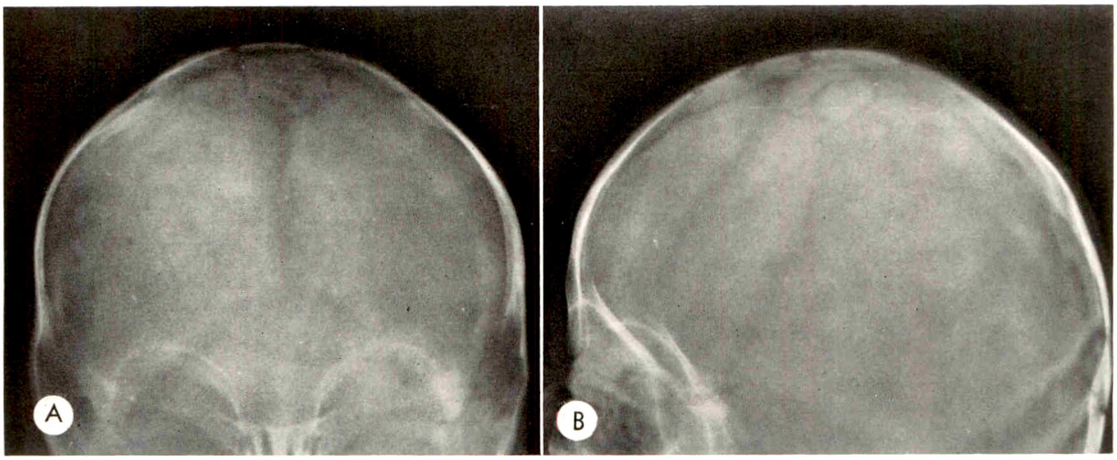

FIG. 2. (*A*) Frontal and (*B*) lateral projections. At least 5 separate bones lie in the anterior fontanel of this boy, who is 5 months of age.

One child at 1 month of age had no bone in his anterior fontanel; at $2\frac{1}{2}$ years of age he had a large bone filling his anterior fontanel and almost wholly fused with the adjacent bones of the skull. Anterior fontanel bones are usually single but were multiple in 2 children (Fig. 2, *A* and *B*). In 3 children a small bone occupied part of the fontanel. The small bone may lie posteriorly (Fig. 3), centrally, or anteriorly. If a metopic suture is present, a bone may lie in it either posteriorly (Fig. 4, *A* and *B*) or anteriorly (Fig. 5, *A* and *B*). Three children had wide metopic sutures with single bones in them. In 2 children with anterior fontanel bones, the metopic sutures were open (Fig. 6, *A–D*). In one child the coronal sutures adjacent to the anterior fontanel were the sites of bones (Fig. 7, *A* and *B*).

As it grows, the intrafontanel bone occasionally remains flat and then does not develop a diploic space as early as do the surrounding bones (Fig. 8, *A–D*).

Fusion between the anterior fontanel bone and the adjacent bones of the skull, the frontal and the two parietals, appears to be complete by the 4th or 5th year of life; no examples of independent fontanel bones were seen in our children older than 4 years. Fusion may first occur posteriorly (Fig. 8, *A–D*) or anteriorly.

Caffey[3] stresses the fact that in the skull "normal variations in the location of the ossification centers and in the patterns of the sutures" are numerous; and that in some apparently normal skulls wormian bones "may be single or multiple, exceeding 100 in number." Dedick and Caffey[5] in their study of the skulls of 1,030 infants and Caffey[4] in examinations of approximately 10,000 newly born infants identified no anterior fontanel bones.

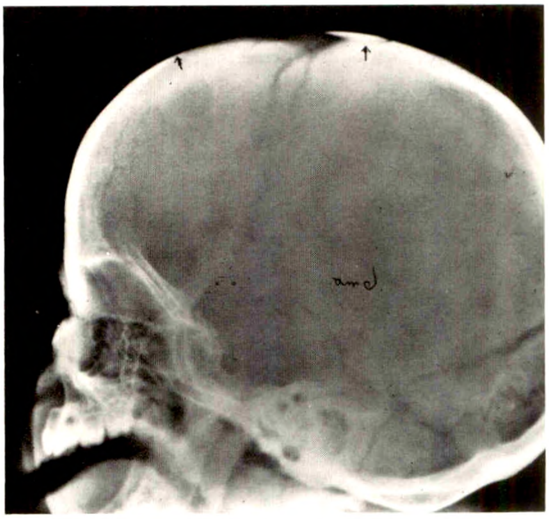

FIG. 3. Lateral projection. The large anterior fontanel of this boy, 6 months of age, contains a small chip of bone (↑). The anterior arrow delineates the anterior margin of the anterior fontanel.

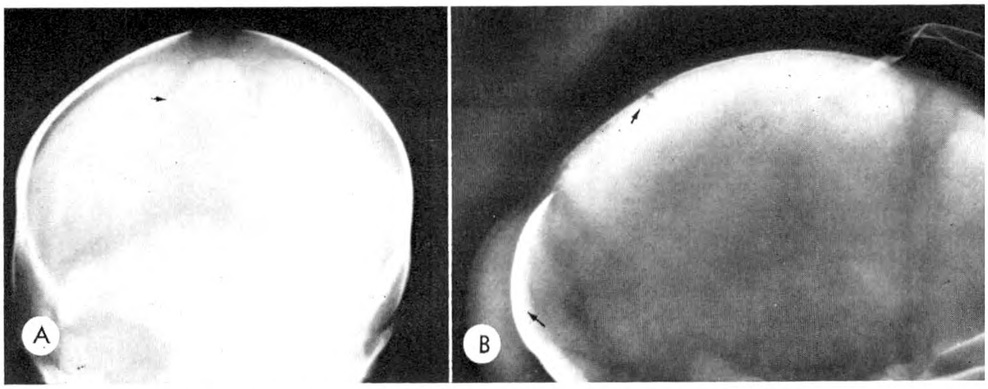

FIG. 4. (*A*) Frontal and (*B*) lateral projections. In this boy, 3 days of age, in the lateral project
bone (→) lies in the region of transition between the anterior fontanel and the wide metopi
occipital cephalhematoma (←) and small parietal foramina (↑) are present. In the frontal p
accessory bones lie well anterior to the anterior fontanel in the metopic suture. The child w
again when he was 20 months of age; neither the accessory bone nor residua of the cephal
parietal foramina were visible. The skull had grown at a normal rate.

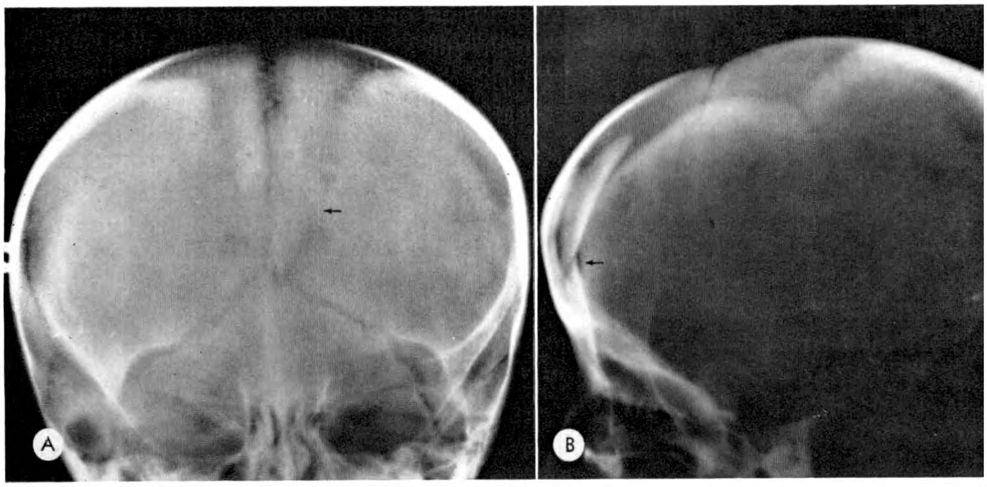

FIG. 5. (*A*) Frontal and (*B*) lateral projections. In the skull of this boy, 14 months of age,
cephalus, a large bifid bone (←) fills the anterior portion of the wide metopic sutur

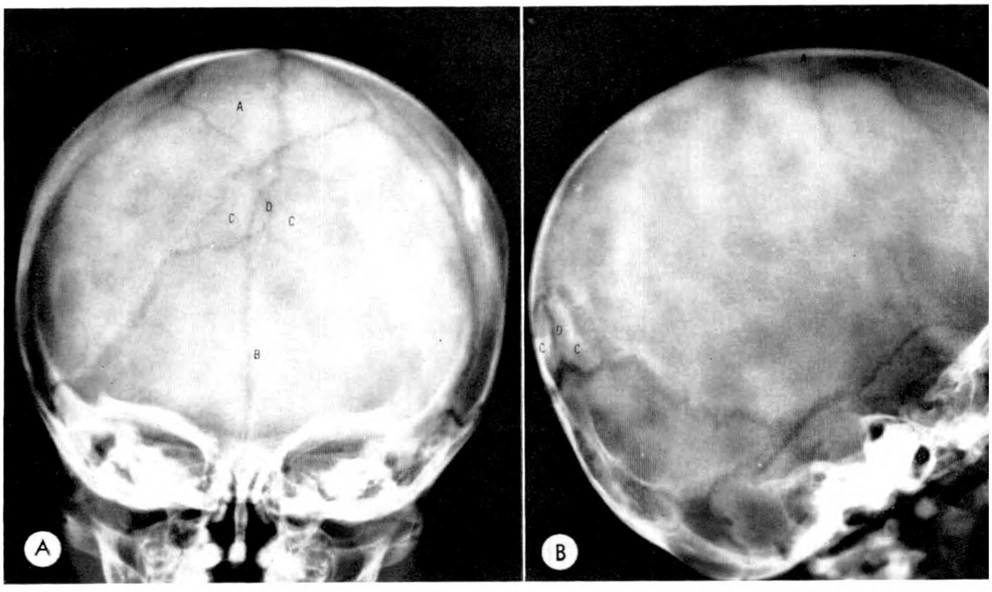

FIG. 6. (*A* and *B*) Frontal and lateral projections. In the skull of this boy, $3\frac{1}{2}$ months of age, a
the anterior fontanel, the metopic suture (B) is patent, and an interparietal bone (C) is
superior median fissure (D).

TUBERCULOSIS OF VERTEBRAL COLUMN
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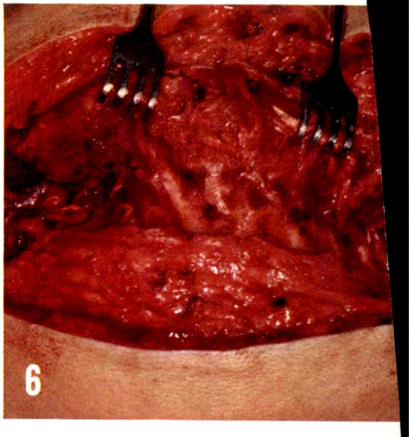
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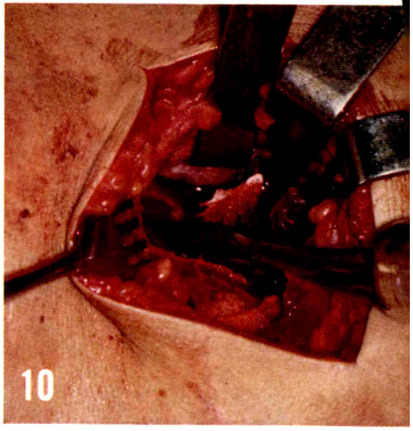
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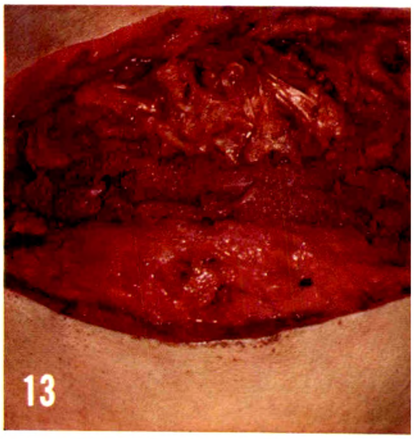
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Figure 6. Right half of vertebral column laid bare by subperiosteal dissection. Right laminae may be seen deep in wound in kyphotic area.

Figure 7. Chip of bone from spinous process being turned down by gouge to bridge interlaminal gap.

Figure 8. Right posterior iliac incision made to obtain bone chips for fusion area at kyphosis.

Figure 9. View of right iliac bone donor site from which chips were taken to reinforce area of fusion.

Figure 10. Bone chip being turned down from right iliac site.

Figure 11. Bone chips on towel taken from right iliac site to reinforce area of fusion.

Figure 12. Cancellous bone grafts packed into right half of vertebral column at time of fusion.

Figure 13. Close-up of surgical area shown in Figure 12.

Figure 14. Wound closure. Dark areas indicate coagulated bleeding points.

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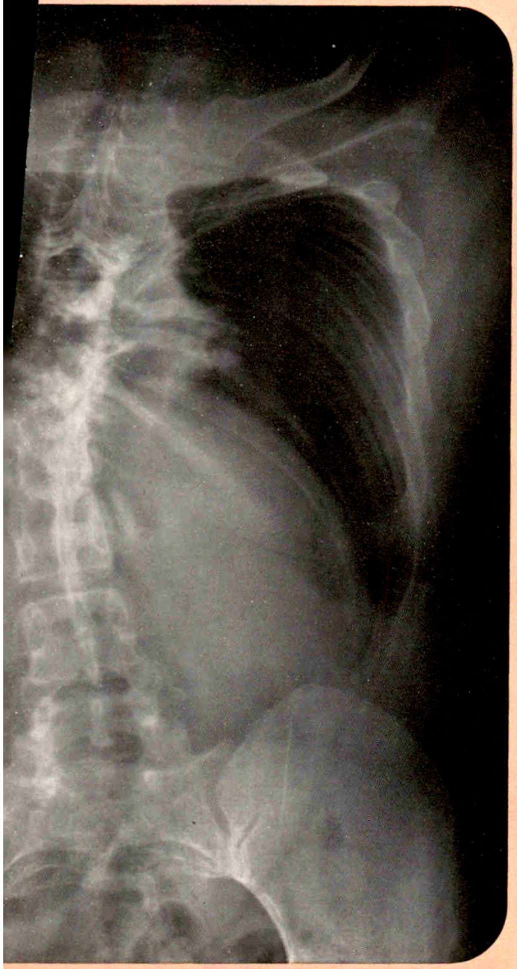
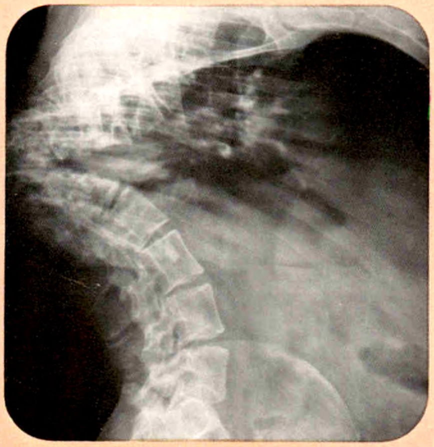
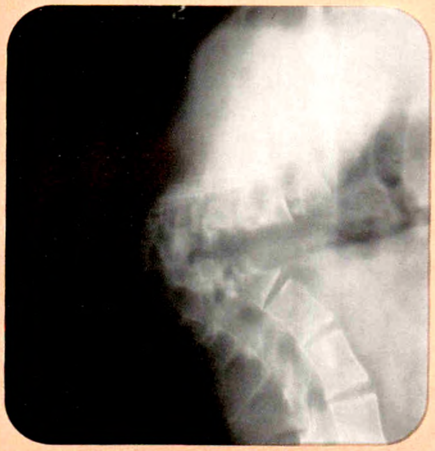


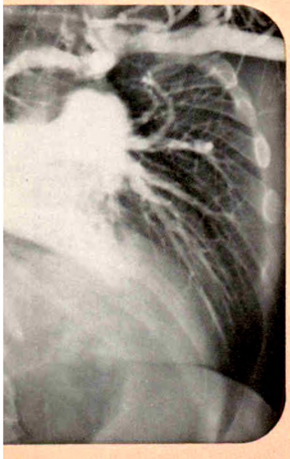
ertebral column showed pronounced vertical shortening
n in lower thoracic vertebrae.



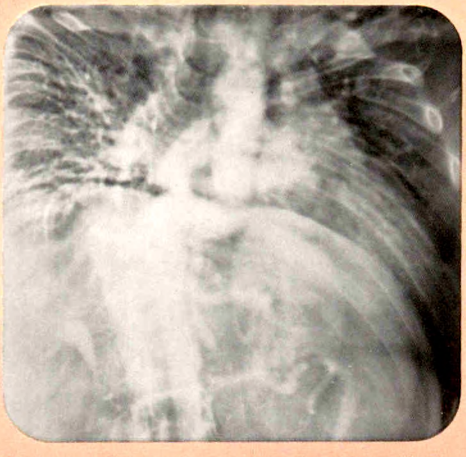
2. Lateral projection showed severe "hairpin" kyphosis, result of vertebral tuberculosis.



3. Lateral tomogram revealed areas of bone destruction and soft-tissue calcification in lower thoracic vertebrae.



showed filling of right cardiac
na cava, and pulmonary arteries.
y is slightly dilated. Compression
e to kyphosis was demonstrated.



5. Angiocardiogram, late in series, showed opacification of aorta with severe buckling and deformity secondary to kyphosis. No tumor mass or large abscess identified.

For details of surgery... TURN PAGE

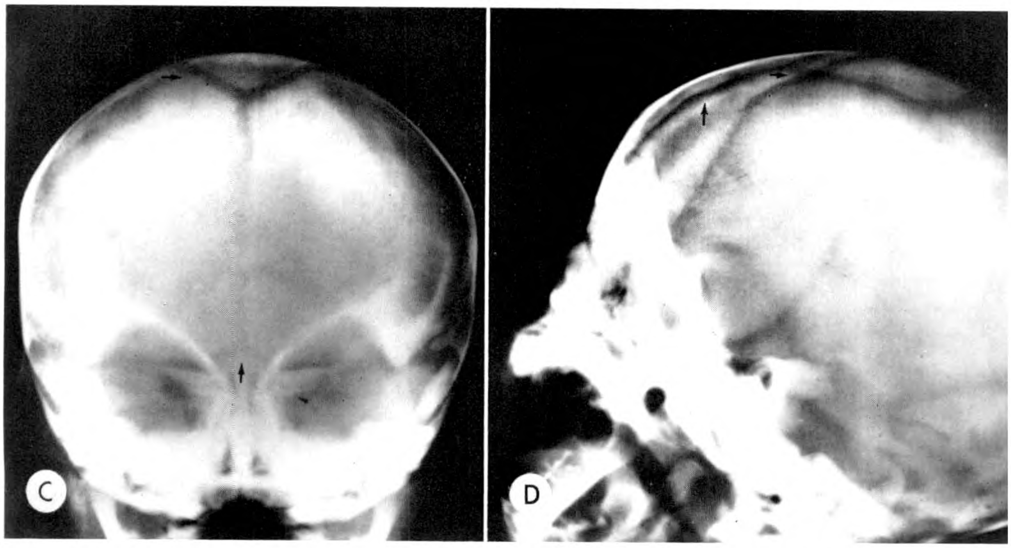


FIG. 6. (*C* and *D*) In another boy, who is 4 days of age, the anterior fontanel contains a larg
(→) and the metopic suture is open (↑).

Torgersen[7] observed no anterior fontanel bones in roentgenograms of the skulls of 400 children older than 5 years. Wormian bones that were visible on gross specimens were not seen on roentgenograms because obliteration of the sutures was too far advanced. In the group of children reported here, the oldest child in whom an anterior fontanel bone was present was 4 years of age.

Caffey,[3] and Schinz and colleag
lieve that the fontanels close thro
growth from the periphery of the
bones and by the development in
new ossification centers.

The usual mechanism for closu
fontanel is centripetal marginal g
contiguous bones until finally the
fontanel is obliterated. Occasio
separate bone appears in the ante

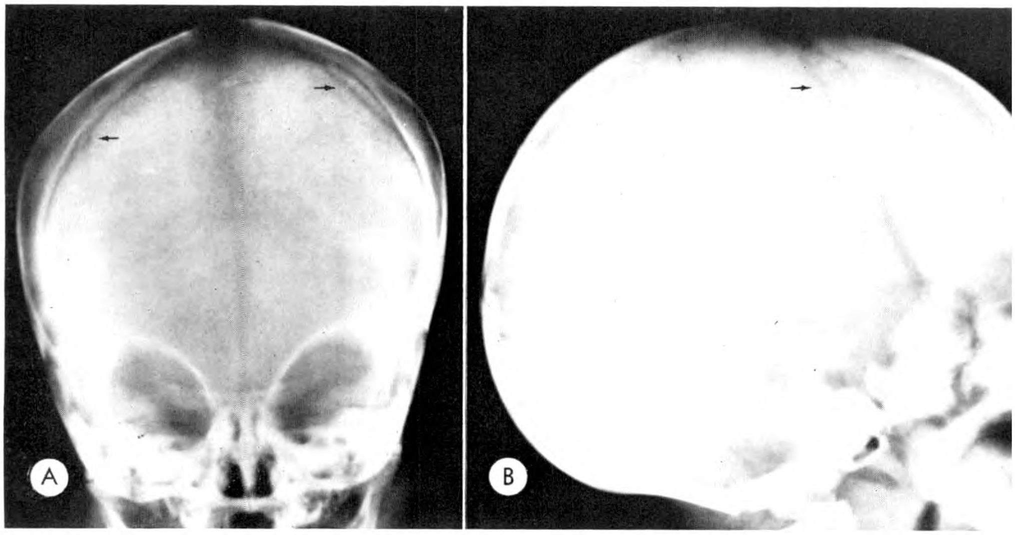


FIG. 7. (*A*) Frontal and (*B*) lateral projections. In the skull of this boy, 3 months of age, a small b
one of the coronal sutures (→) and an even smaller bone lies in the other coronal suture (←). Th
fontanel does not contain a bone.

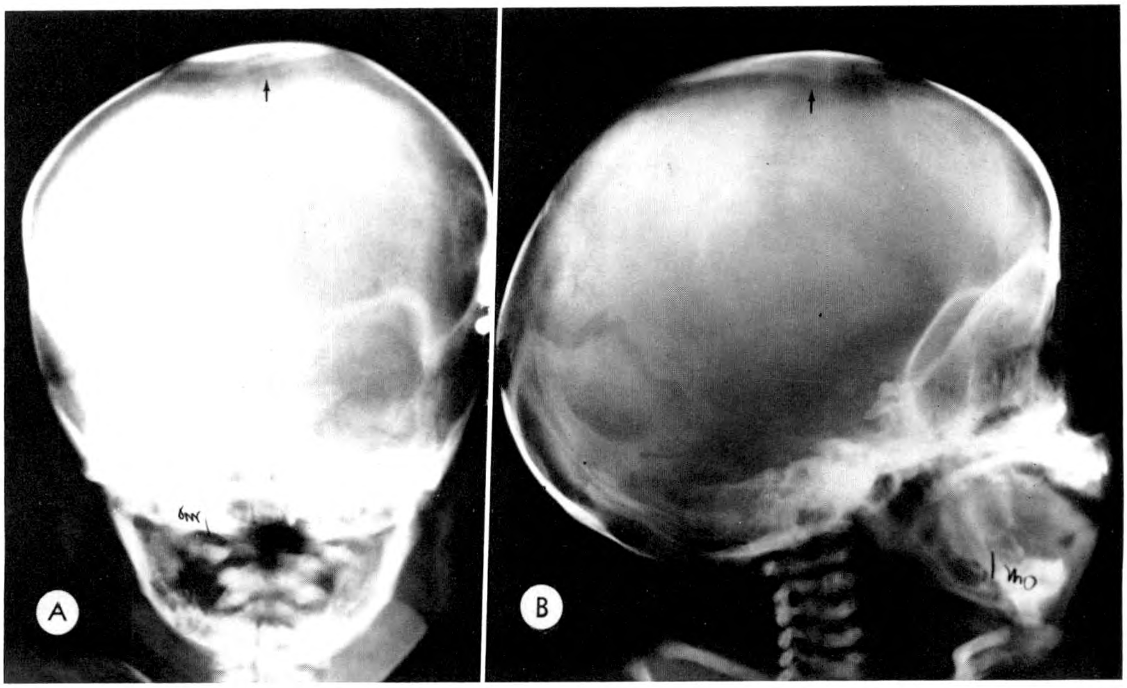


Fig. 8. (*A* and *B*) Frontal and lateral roentgenograms of the skull were made when this girl was 1 month of age.

tanel before or after birth. This separate bone appears to grow centrifugally until it fuses in variable sequence with the centripetally growing edges of the parietal and frontal bones during the 4th or 5th year of life. The anterior fontanel bone does not interfere with the normal growth of the skull, nor does it alter the pattern of abnormal growth in the case of tumor or hydrocephalus.

Bones in the anterior fontanel and its contiguous sutures should be recognized as normal variants. Otherwise, they may wrongly suggest premature closure of the

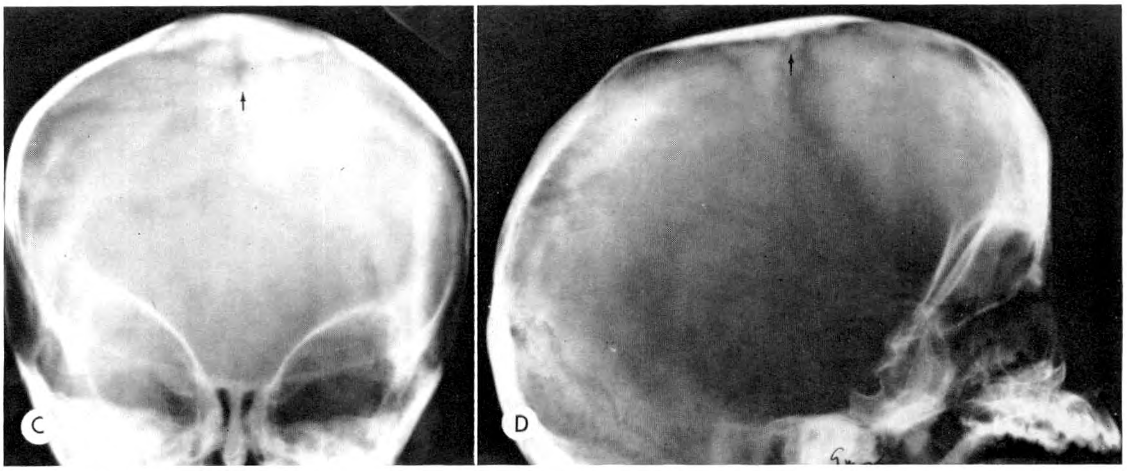


Fig. 8. (*C* and *D*) Same girl 8 months later. Growth of the skull has taken place at a normal rate. The bone in the anterior fontanel (↑) has become flat and has not developed a diploic space. Fusion has occurred posteriorly.

fontanel to the pediatrician and premature closure of the fontanel or fracture of the parietal or frontal bones to the radiologist.

SUMMARY

Bones in the anterior fontanel and its contiguous sutures are normal and relatively common variants that do not interfere with normal growth of the skull. The bone is usually single. It is occasionally flat and may or may not develop a diploic space. Fusion between the fontanel bone and the surrounding bones of the skull occurs usually before the 5th year of life.

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NORMAL AND ABNORMAL INTERORBITAL DISTANCES, WITH SPECIAL REFERENCE TO MONGOLISM*

By BARRY E. GERALD, M.D.,† *and* FREDERIC N. SILVERMAN, M.D.
CINCINNATI, OHIO

MONGOLISM, as a clinical entity, was first described in detail by Down in 1866.[9] Roentgenographic stigmata of the disease were recognized by Clift[5] in 1922. He described a small, dolichocephalic skull with thin bones and separation of the cranial sutures. He also recognized the poor development of the nose and maxilla. Interest in the roentgenographic signs of mongolism received impetus with the description by Caffey and Ross[3] of the bony pelvis in the syndrome, which permitted a roentgenographic diagnosis in the first months of life when clinical diagnosis is most difficult.

The purpose of this paper is to present a new roentgenographic sign in mongolism, specifically, narrowing of the interorbital distance (orbital hypotelorism). We suggest that orbital hypotelorism is the skeletal substrate for the characteristic facies of the patient with Down's syndrome or mongolism.

METHODS AND MATERIALS

The interorbital distance was first defined by Cameron,[4] a physical anthropologist, in studies of a small number of dried skulls. He described this dimension as the maximal distance between the medial walls of the bony orbits, measured at the juncture of the crista lacrimalis posterior with the fronto-lacrimalis suture (Fig. 1). The interorbital distance was described roentgenographically by Currarino and Silverman[6] in their studies of arhinencephaly and trigonocephaly. In an attempt to duplicate as closely as possible the work of Cameron, the interorbital distance was determined by measurements on posteroanterior roentgenograms of what was believed to represent the junctures of the medial angular processes of the frontal bone with the maxillary and lacrimal walls. Basically, this defines the distance between the anterior portions of the lateral ethmoidal walls which is also the distance between the anterior edges of the lamina papyracea.

To establish their original standards, Currarino and Silverman[6] used nonrotated posteroanterior roentgenograms of skulls obtained at a target-table top distance of 100 cm. and a patient-film distance of 5 cm. The roentgenograms of 250 patients of varying ages from birth to 12 years were studied. The majority had been examined for suspected fracture or sinusitis and were otherwise normal. A distribution diagram was constructed showing the mean values with a range of 3.291 standard deviations above and below because of the limited number of measurements in each age group.

In order to provide statistically more reliable standards, the original study of Currarino and Silverman[6] has been repeated using the same technical factors and patient selection but surveying 100 patients in each year of age from birth through 12 years. The previous study had found no significant relationship between the interorbital distance and the patient's sex so that age was the single factor considered. Although correlation with the patient's physical measurements would be of interest, this was beyond the scope of this study.

In the older child with a well pneuma-

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* Presented at the Sixty-fifth Annual Meeting of the American Roentgen Ray Society, Minneapolis, Minnesota, September 29–October 2, 1964.

From the Departments of Pediatrics and Radiology, University of Cincinnati College of Medicine, The Children's Hospital, and The Children's Hospital Research Foundation.

This work was made possible in part through NIH Grant FR-00010.

† Present address: Children's Hospital of the East Bay, Oakland, California.

tized ethmoid, roentgenographic differentiation between the anterior portions of the ethmoid at the level of the lacrimal bones and the ethmoid cells lying adjacent to the more laterally placed posterior orbital walls may be difficult (Fig. 2). In most cases, however, the medial orbital rim forms a smooth inferiorly directed curve continuous with the anterior portion of the ethmoidal wall and the interorbital distance can be determined adequately. Any but the most minor degrees of rotation will make evaluation difficult.

The roentgenograms of 112 patients with a clinical diagnosis of mongolism seen at The Children's Hospital and at the Hamilton County Diagnostic Clinic for Retarded Children were then reviewed. The interorbital distance was determined in those patients having satisfactory posteroanterior roentgenograms of the skull. Forty-six satisfactory roentgenograms were available for study. All of the measurements were made to the nearest millimeter. Chromosomal analyses were not available from a sufficient number of patients to permit analysis of the effect of genotype on orbital measurements, but no gross differences were noted in the several types of mongolism (trisomy 21, mosaicism, and translocation) in the few patients with available karyotype analyses.

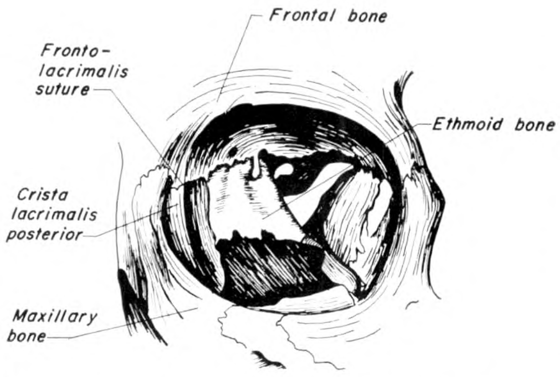

Fig. 1. Anatomy of orbit to show point of reference for measurement of interorbital distance. (Adopted from Sobotta, J. Descriptive Human Anatomy. Hafner Publishing Company, Inc., New York, 1954.)

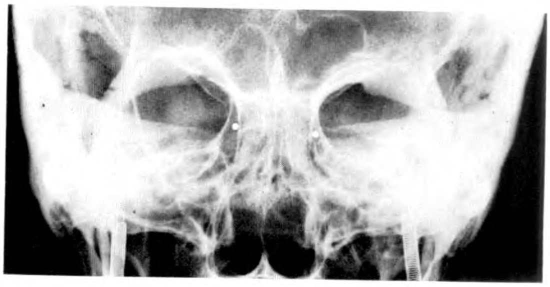

Fig. 2. Roentgenogram of skull (anatomic specimen) with metallic markers at juncture of crista lacrimalis posterior with the fronto-lacrimalis suture. Note that the smooth curve is continuous with the medial rim of the orbital margin. The interorbital distance would be measured between the medial edges of the metallic markers.

RESULTS

The mean interorbital distance in the normal patients as well as the 5th and 95th percentile levels is presented graphically in Figure 3. The interorbital distances of the patients with mongolism are superimposed.

To determine the accuracy with which a given interorbital distance may be termed normal or abnormal, Table 1 is presented.* This compares the normal with the mongoloid in each age group. As presented, a measurement greater than the critical value is likely to be that of a normal patient with a probability of, at least, 78 per cent; conversely, a measurement below the critical value is likely to be that of a patient with mongolism with a probability of, at least, 78 per cent. The lower the interorbital distance in relation to the value given, the greater the accuracy of predicting abnormality. An error of not more than 22 per cent can be expected but this error will decrease as the deviation from the given value increases. The upper level of the normal range has not been established. Therefore, the presence or absence of orbital hypertelorism cannot be determined with the table.

The interorbital distance in a normal patient increases in a regular fashion up to ap-

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* The analysis of the data is based on statistical least square estimating techniques. The statistical treatment is discussed at greater length in the appendix.

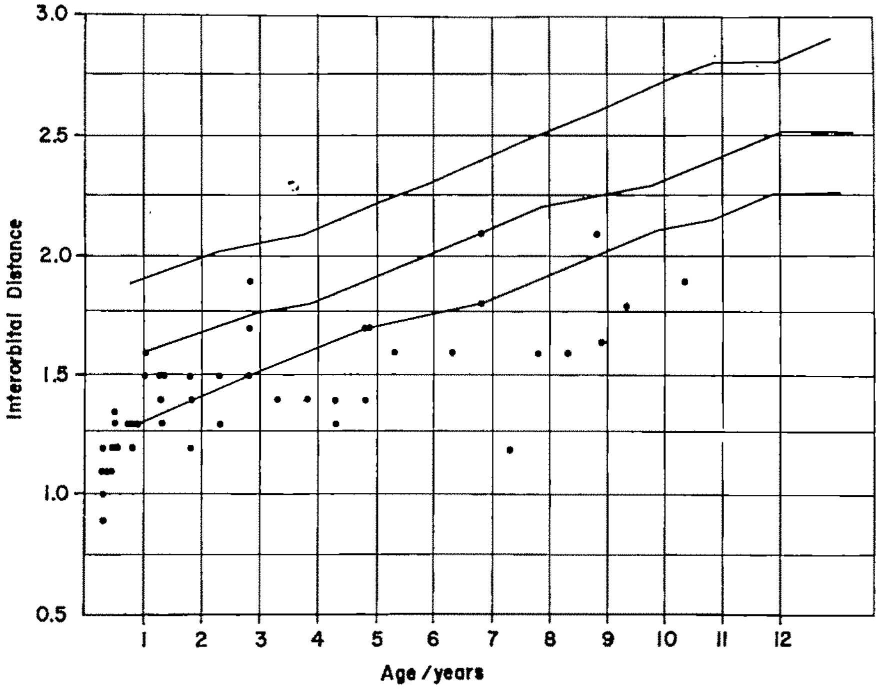

FIG. 3. Unsmoothed curves of normal interorbital distances (in centimeters) and distribution of measurements of mongols.

proximately age 9. There is a short lived increase in the annual increment at this time and the maximal values for interorbital distance are reached by 11 to 12 years in the group studied. This prepubertal growth acceleration is similar to that found in somatic growth. As is well known, the growth of the brain does not follow this pattern but rather increases rapidly during the first year of life and then decelerates rapidly with 80 per cent of mature size obtained by the age of 4 years. The apparent increase in the size of the skull after brain growth has ceased is due to pneumatization of the frontal sinuses, increase in the diploic space and increased thickness of the soft tissues. Increase of the interorbital distance as a function of somatic growth, rather than of brain growth, indicates that the ethmoidal region increases in width independent of the brain in the normal patient.

The interorbital distance with mongolism is significantly decreased in the majority of cases. However, the mean distance does appear to increase with age although it is significantly below the mean for normal patients. Seward *et al.*[15] have demonstrated that the breadth and length of the mongo-

TABLE I

INTERORBITAL MEASUREMENTS AT VARIOUS AGES WHICH SEPARATE PATIENTS WITH MONGOLISM FROM NORMAL INFANTS AND CHILDREN WITH A PROBABILITY OF 78 PER CENT

Age (mo.)	Critical Level (cm.)
3	1.45
6	1.47
9	1.49
12	1.50
24	1.57
36	1.63
48	1.70
60	1.76
72	1.83
84	1.90
96	1.97
108	2.01
120	2.10
132	2.16
144	2.23

loid cranium increased at nearly normal rates after age 5 to 8 but rarely attained the dimensions of a normal patient. Central facial hypoplasia in mongolism was first described by Clift[5] and in greater detail by Benda[2] who described the nasion, ethmoid, maxillae, and portions of the sphenoids as small.

DISCUSSION

A decrease in the interorbital distance was originally described by Currarino and Silverman[6] in association with arhinencephaly and with simple trigonocephaly (Fig. 4, *A–D*). For this finding, they coined the term hypotelorism. Orbital hypotelorism is differentiated from ocular hypotelorism which refers to measurements of the interpupillary distance although the two may coexist. The term arhinencephaly included a group of malformations with almost uniformly bilateral absence of the olfactory nerve, the most severe form being cyclopia and the least severe, arhinencephaly with trigonocephaly. This group of malformations has been further discussed by DeMyer and associates.[7,8] To better describe the basic malformation, failure of division of the prosencephalon, the term holoprosencephaly was suggested. Three groups could then be distinguished, depending upon the degree of midline separation of the cerebral cortex. The first, the *alobar* form, included cyclopia, ethmocephaly, cebocephaly and arhinencephaly with median cleft lip. This latter is the most commonly observed of these malformations because it is not incompatible with survival for some months. The second group, *semilobar* holoprosencephaly, is a less severe defect, allowing the patient to survive into childhood but associated with a fairly severe degree of amentia. The corpus callosum as well as the olfactory bulbs and tracts may be absent and a dorsal cyst may be present, but neither of the latter two is required for the diagnosis. The third group, *lobar* holoprosencephaly, includes patients who tend to survive infancy and childhood. All are mentally retarded but may be able to function in society. The only manifestations may be aplasia of the olfactory tracts, absence or hypoplasia of the corpus callosum and/or the presence of a dorsal cyst. Often clefts of the lips and palate are present. Some of these malformations have been described in association with trisomy 13–15 syndrome.[11] The less severe forms of alobar holoprosencephaly are associated with a marked degree of orbital hypotelorism. No definitive statement about the facial malformations in the semilobar and lobar groups can be made. Other malformations of the forebrain and central facial structures may also be associated with orbital hypotelorism. This is shown in Rosen and Gitlin's report[14] of a patient with a bilateral nasal proboscis in association with agenesis

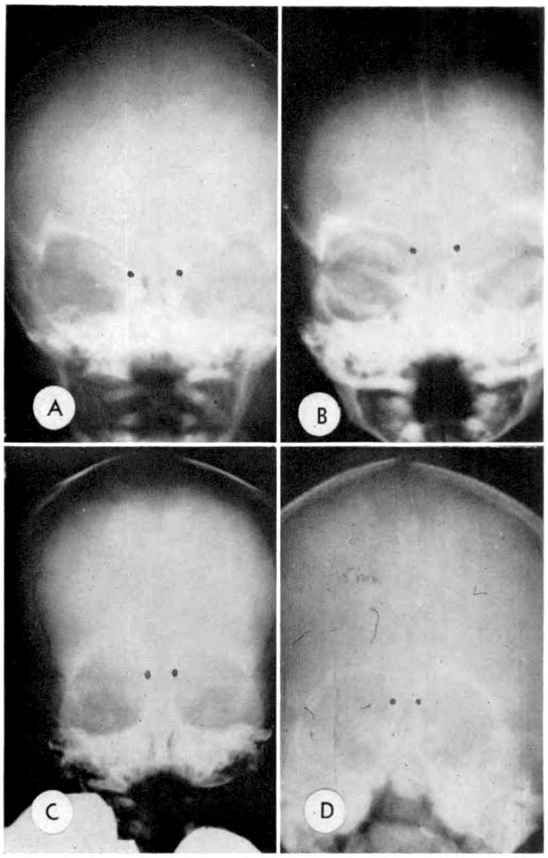

FIG. 4. Representative roentgenograms of infants under 1 year of age. (*A*) Normal; (*B*) mongol; (*C*) trigonocephaly; and (*D*) arhinencephaly with median cleft lip. (*D* is slightly magnified; all other roentgenograms are comparable to each other.)

of the corpus callosum and a large hamartoma of the forebrain. Orbital hypotelorism was demonstrated on postmortem roentgenograms.

The implications of orbital hypotelorism in simple (associated with no demonstrable malformations of the forebrain) trigonocephaly are different from the above. In these patients there is premature closure of the metopic suture either *in utero* or shortly after birth, coupled with hypoplasia of the ethmoid region as shown by the presence of orbital hypotelorism. Apparently, both malformations are required to produce the associated changes in the frontal bone and medial portions of the orbital rims. The frontal region becomes keel shaped with a sharp bony ridge at the level of the closed metopic suture. The orbits assume an oval or egg shape with the longer axes extending upward and medially from the inferolateral margins. The medial orbital walls are almost vertical with loss of the usual medial convexity. This configuration has been described picturesquely as the "surprised coon" appearance[1] because of its resemblance to the periorbital markings of the American raccoon (Procyon lotor).

Although it has been shown that the interorbital distance in a normal patient is a function of facial growth rather than brain growth, the foregoing has shown that abnormal growth of the ethmoidal region can be associated with malformations of the forebrain as well as with changes in the metopic suture. However, in mongolism, the cranial sutures, particularly the metopic, close late.[18] No malformations of the forebrain have been described in the syndrome. Thus, the mechanism of the orbital hypotelorism must for the present be explained by primary hypoplasia of the central facial structures as described by Benda.[2]

We have recently examined a patient with proven mongolism who, in addition, showed the typical keel shaped configuration of the frontal bone seen in trigonocephaly. Roentgenograms demonstrated orbital hypotelorism. However, the metopic suture was closed, an unusual finding in mongolism. This again illustrates that both factors, premature closure of the metopic suture and hypoplasia of the ethmoid region, must be present to produce the clinical picture of trigonocephaly.

The superior obliquity of the lateral palpebral fissures has been the clinical hallmark of mongolism since Down described these patients as "representative of the great Mongolian race" in his original article in 1866.[9] The term mongolism is particularly poor, not only because of its inaccurate description as shown so well by Benda[2] but because of its unintentional stigmatization of persons of Oriental extraction. The eponym, Down's syndrome, has been suggested, but the original term is so ingrained that the effort to change seems futile and the term mongolism is used throughout this article. The characteristic facial appearance is less prominent as the patient grows older. Epicanthal folds, present in many normal newborns but exaggerated and persistent in mongoloids, are rarely seen after the age of 9 or 10 years. The obliquity of the palpebral fissures also seems to decrease but persists to some degree.

A mongoloid appearance of the palpebral fissures is also seen in some forms of holoprosencephaly and in simple trigonocephaly, conditions also associated with orbital hypotelorism.[6] Benda[2] has related the appearance of the palpebral fissures in mongolism to a characteristic superior obliquity of the bony orbital rim at its lateral margin. This characteristic appearance has not been confirmed by other observers. Neither can it be the mechanism in patients with simple trigonocephaly in whom the most superior portion of the orbit is at the medial margin producing the "surprised coon" appearance. Inferior obliquity of the palpebral fissures or an antimongoloid slant is characteristic of patients with hypoplasia of the *lateral* facial structures or the Treacher Collins syndrome. Our observation suggests that the appearance of the palpebral fissures in mongoloid patients is a manifestation of relative hypoplasia of the *central* facial structures in relation to the more normal lateral structures, which is indicated by the roentgenographic finding of orbital hypotelorism. The relative hypoplasia may also be the basis for the persistent epicanthal folds in both mongolism and trigonocephaly. The decreased size of the bony structures causes the relatively hyperplastic overlying cutaneous tissues to pile up into loose folds. As this relative disproportion decreases with increasing age, the loose folds gradually become more taut. A clinical parallel is found in achondroplasia in which the skin overlying the short bones of the extremities is often drawn into extensive folds during infancy.

The disharmony between overlying skin and bony substrate would explain the mongoloid appearance of patients with trigonocephaly and holoprosencephaly in whom there exists the same relative hypoplasia of the central facial structures in relation to the lateral structures. The antimongoloid appearance of the palpebral fissures in patients with Treacher Collins syndrome would then be due to the reverse relative proportions. The data presented by Roche *et al.*[13] as well as in this study show that the mongoloid facial and cranial dimensions more nearly approximate the norm with advancing age. This change is manifested clinically by loss of the characteristic facial appearance and is in accord with our explanation.

Orbital hypotelorism is basically a manifestation of decreased growth of bone in the ethmoidal region. Speculation as to its occurrence in disease states other than mongolism and the arhinencephalic group of malformations is of interest. Certain forms of microencephalic microcrania might also show a decreased interorbital distance as a result of diminished growth of the cranium. Patients with a generalized decrease in body growth, as occurs classically in hypopituitarism, could have a decrease in interorbital distance unrelated to growth of the brain. The absence of mongoloid facies would be expected in these two groups as decreased growth is not confined to the central facial structures. Whether orbital hypotelorism occurs commonly in the trisomy 13–15 group is not known but might well be confined to those with malformations of the forebrain. Future observations along these lines will be informative.

SUMMARY

1. The interorbital distance of normal children, as determined roentgenographically, has been measured using a larger number of samples than previously reported. This allows more accurate standards than available before.

2. The interorbital distance in a group of 46 patients with mongolism, or Down's syndrome, has been determined and is shown to be significantly decreased in the majority of patients, indicating orbital hypotelorism.

3. Orbital hypotelorism in mongolism, as in arhinencephaly and/or trigonocephaly, is apparently secondary to primary hypoplasia of the central facial structures.

4. Evidence has been presented suggesting that the upward obliquity of the lateral palpebral fissures and the persistent epicanthal folds in mongolism are secondary to relative hypoplasia of the bony central facial structures.

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APPENDIX

As can be seen from the figures in the body of the paper, interorbital distance, D, is a well behaved function of age. Serving as basis for a decision function which will help to separate normals from mongols is the best estimate of D for normals, D for mongols, and errors of estimate for interorbital distances for both normals and mongols. Since the hypothesis that interorbital distance is a linear function of age seems quite acceptable from the data, an estimating equation for interorbital distance for both normals and mongols was easily obtained using the techniques of least square curve fitting.

The prediction for D for normals was as follows:

$$D_n = .006 \text{ (age in months)} + 1.5851$$

and the standard error of prediction for normals, S_n

$$S_n = .1968.$$

The best estimate for mongols interorbital distance, D_m

$$D_m = .005 \text{ (age in months)} + 1.2663$$

with standard error of prediction for mongols, S_m

$$S_m = .2223.$$

This information may now be used to examine the two possibilities, namely, that a particular child is normal and that a particular child is a mongol. A probability can be computed for either decision being the correct one and of the child deviating from either normal or mongol interorbital distances by chance alone.

Where X is an interorbital measurement on a child, we find the probability of error for the hypotheses that the child is either normal or abnormal by determining the distance from the best estimated interorbital distance the child ought to have if he were either normal or mongol. The probability associated with observing a deviation as large or larger from expectation may then be looked up in a table of the normal curve.

To find the probability that the child's interorbital distance deviates from normal expectation we first find Z_n

$$Z_n = \frac{D_n - X}{.1968},$$

the probability associated with Z_n is then looked up in a table of normal probability.

To find the probability that the child is a chance deviation from a mongol we find Z_m

$$Z_m = \frac{X - D_m}{.2223},$$

where the probability corresponding to Z_m is looked up in a table of the normal probability.

For example, let us say we had a child that was 80 months old and has an interorbital distance measure of 1.9 cm. Our best prediction for the child's interorbital distance if it were normal, D_n, is equal to 2.0651 cm. and if it were abnormal, D_m, is equal to 1.6663 cm. If the child should be normal, then the probability that 1.9 cm. is a chance deviation from 2.0651 cm. is given by

$$Z_n = \frac{.1651}{.1968} = .84.$$

The probability of getting an interorbital distance as small as 1.9 or smaller by chance alone on a normal child is equal to .2.

If we assume that the child is a mongol then the probability that we will obtain a measurement of 1.9 or larger by chance alone is given as follows:

$$Z_m = \frac{.2337}{.2223} = 1.05.$$

The probability of having a mongol child deviating by chance from the expected value of 1.6663 is approximately equal to .16.

The weight in this child's case would indicate a very slight preference for the decision that the child is mongol. This particular calculation has to be considered in relation to other clinical findings. Of course, if the interorbital distances are very very small or very very large, then the decision that the child is either mongol or normal may be based directly on his or her interorbital distance.

A quick rule of thumb was also devised and is used in the text. Based on the similarity in slopes for normals and mongols, the assumption was made that the slope for normal or mongol interorbital distance by age was really the same. Assuming that the estimates, in these data, of the standard error of the distributions of estimates are a good approximation of the true distribution, we can then think of a line being drawn through those points for all age groups which divide our error distribution such that an equal number of normals or abnormals will fall on either side of this line. The line selected was for an interorbital distance such that the probability of a correct choice or incorrect choice was the same for normals or abnormals. The equation itself was

$$L = .0055 \text{ (age in months)} + 1.4353,$$

where L is the line of division between mongols and normals. The rule to be followed is that if the interorbital distance obtained is larger than L the child is called normal and if smaller than L the child is called abnormal. The probability of correct choice for such a rule is 78 per cent and the probability of error, of course, is 22 per cent for either decision if the child is normal or abnormal.

It is obvious that as a rule of thumb the second alternative has the weakness that a very small or very large interorbital distance carries the same importance to the clinician as an intermediate interorbital distance. We think that the application of the exact calculations as outlined previously may be much more valuable since in doubtful cases such calculation may give enough reason to throw an opinion one way or the other, well based on known probabilities.

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DIAPHYSEAL DYSPLASIA

REPORT OF A CASE

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DIAPHYSEAL hyperostosis, or diaphyseal dysplasia, as it is more commonly designated, is an uncommon pathologic entity with specific and striking roentgenographic findings.

In recent years, there have been several reports summarizing the literature so that a detailed review at this time would be repetitious. The case here reported is of interest not only because of the rapid and marked progression of the lesions but, also, because of the extensive skeletal involvement with subluxation of the radial heads and marked involvement of the calvarium, necessitating decompression.

These patients have few major complaints. They are usually malnourished and have muscular weakness and fatigue. The gait has been reported as wide-based or waddling. No specific laboratory findings have been recorded. There is gradual symmetric sclerosis and fusiform widening of the diaphyses of the long bones secondary to hyperostosis. The zones of hyperostosis are usually sharply demarcated from the normal bone in the metaphyses. This process commonly spares the metaphyses and epiphyses; in 2 case reports involvement of the femoral capital epiphyses and metaphyses was described. Eventually, no normal trabeculation remains, and, within the thickened and sclerotic bone, there are mottled areas of rarefaction.

The skull may show sclerosis and thickening, most often in the base, with later involvement of the vault, usually in the frontal area. The facial bones, mandible and spine are generally not affected, although Schinz showed roentgenograms with involvement of these bones reportedly in patients with diaphyseal hyperostosis. The ribs, scapulae, pelvis, clavicles, hands and feet are infrequently involved.

The rate of progression varies considerably, although, in reviewing the reported cases, it was noted that progression usually occurs in the younger patients, and the bone changes tend to stabilize in older patients.

REPORT OF A CASE

P.G., a white female, now 14 years old, was first seen at 2½ years of age when she came to the radiology department for roentgen study of her legs because of vague pains. Roentgenograms showed the bone changes typical of a diaphyseal dysplasia.

She is the youngest of 5 children. The parents and siblings are normal and there is no history of any "bone disturbances" in the family. She appeared normal at birth but had difficulty thriving and was treated for anemia and malnutrition by the family physician. She had a waddling gait when she started to walk at 15 months. There was some pain in the thighs when she was referred for roentgenologic consultation.

FIRST ROENTGEN EXAMINATION. This was made at the age of 2½ years. The following were the findings:

Extremities (Fig. 1; and 2, *A* and *B*). Marked sclerosis and thickening of the diaphyses of the long bones with periosteal layering were demonstrated. The mid-portions of the bone showed the most extensive involvement with the metaphyses being unaffected. There was sharp demarcation between the involved diaphyses and the metaphyses. The hands and feet were not involved.

Flat Bones. These were negative except for a slight increase in the density of the clavicles centrally and a coarse pattern in the acromion processes.

Pelvis and Spine. A coarse trabecular pattern was demonstrated in the pelvis and several of the lower lumbar vertebrae but no sclerosis was noted.

Skull. The skull showed minimal sclerosis in the floor of the anterior and middle fossae (Fig. 3).

She was treated symptomatically without any improvement in the anemia or malnutrition.

SECOND ROENTGEN EXAMINATION. At the age of 4½ years, follow-up studies showed the following changes:

Extremities (Fig. 4 and 5). Marked and striking increase in the fusiform widening of the shafts with loss of trabeculation was demonstrated. In the femora there was marginal cortical irregularity and marked mottling. In the radius and ulna, the bone changes extended into the upper metaphyses. The uninvolved bones appeared osteoporotic.

Flat Bones. Further progression of the clavicular sclerosis was noted. The ribs showed widening, cortical thickening and sclerosis.

Pelvis and Spine. Studies showed minimal sclerosis.

Skull. A definite increase in the extent of the sclerosis, involving the base of the skull in the anterior and middle fossae, was seen.

FURTHER COURSE. At 8 years of age there were progressive changes, the most marked

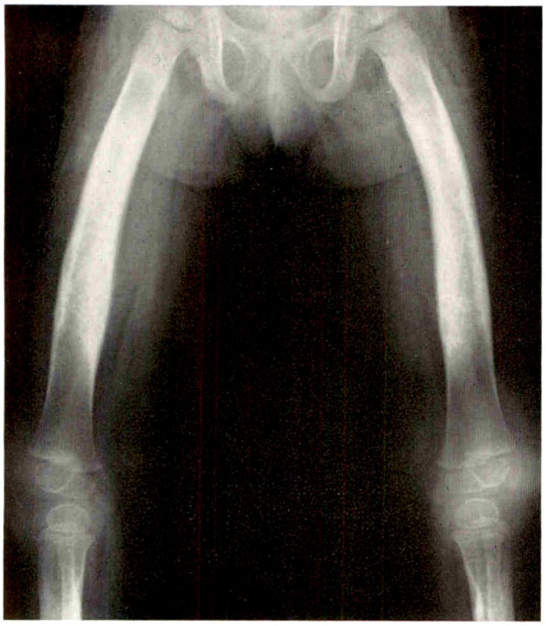

Fig. 1. Aged 2½ years. Early symmetric thickening and sclerosis of the diaphyses of the femora are demonstrated. Similar changes were present in the arm bones.

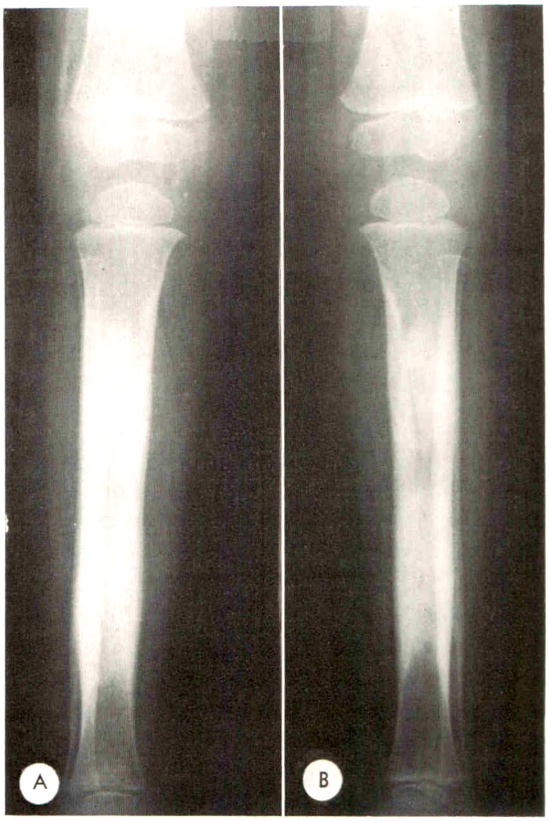

Fig. 2. (*A* and *B*) Roentgenograms showing symmetrical thickening and sclerosis of the tibiae and fibulae.

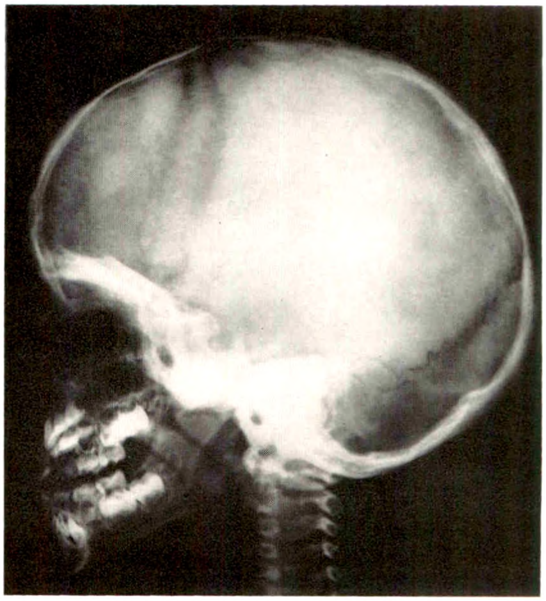

Fig. 3. Aged 2½ years. Minimal sclerosis of the floor of the anterior and middle fossae.

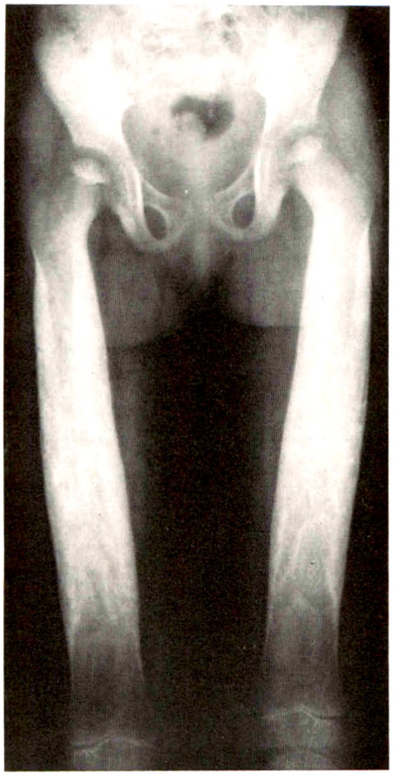

FIG. 4. Aged 4½ years. Progression of the diaphyseal lesions of the femora. Compare with Figure 1.

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being an increase in thickness of the calvarium with sclerosis, especially in the frontal, parietal and basilar regions. The mandible and face were uninvolved. A coarse trabecular pattern was demonstrated in many of the vertebral bodies. The extremities showed progressive involvement.

By the age of 10 years, the patient weighed only 56 pounds and was 50 inches tall. The skull circumference measured 57 cm.

Muscle tone was very poor and the patient tired easily. She had varicose veins in both legs. She walked stiff-legged and had limited dorsiflexion of the feet.

There was a mild proptosis and papilledema of the fundi. The tonsils and adenoids were enlarged and she had a serous otitis with impaired hearing. There was shotty enlargement of the cervical, inguinal and axillary lymph nodes. A tonsillectomy, adenectomy and a bilateral

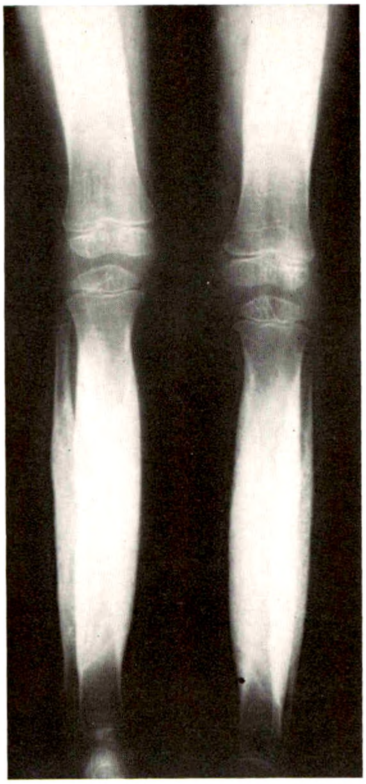

FIG. 5. Progression of the diaphyseal lesions of the tibiae and fibulae. Compare with Figure 2.

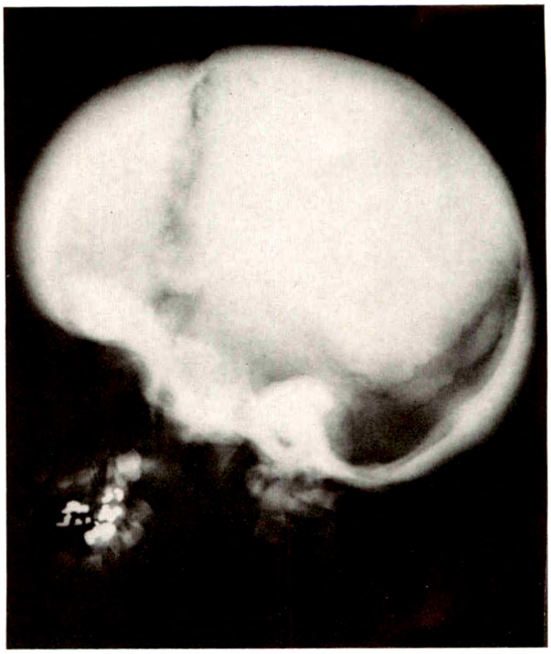

FIG. 6. Aged 10 years. Extensive involvement of calvarium associated with slight proptosis and papilledema. Compare with Figure 3.

myringotomy were performed with improvement in hearing.

THIRD ROENTGEN EXAMINATION. At the age of 10 years, the roentgen findings were as follows:

Skull (Fig. 6). Very marked sclerotic thickening of the calvarium, particularly in the frontal and parietal bones, was demonstrated. During the previous 2 years, the progression of the diaphyseal dysplasia became more marked in the skull than in the other bones. Cerebral arteriograms were made because of papilledema and these were normal.

She then had a bilateral temporal decompression. The neurosurgeon found that the temporal muscles were largely replaced by fibrous tissue and very thin. The underlying bone was very irregular, moderately vascular and very thick, making removal difficult. The brain showed marked tension.

The pathologist reported extremely dense bone with small amounts of fibrous tissue in the interstices. No abnormalities were noted in the bone cells or matrix. A bone marrow smear from the iliac crest showed "active myelo- and erythropoiesis." Laboratory studies showed values within the normal range for blood proteins, calcium, phosphorus and alkaline phosphatase.

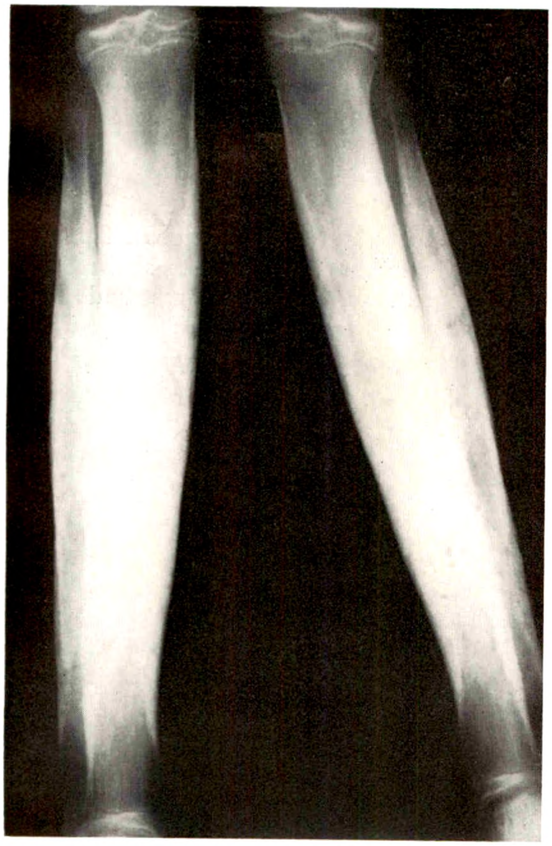

Fig. 7. Aged 12½ years. Genu valgum with further mottled sclerosis and thickening of the tibial and fibular diaphyses. Compare with Figure 5.

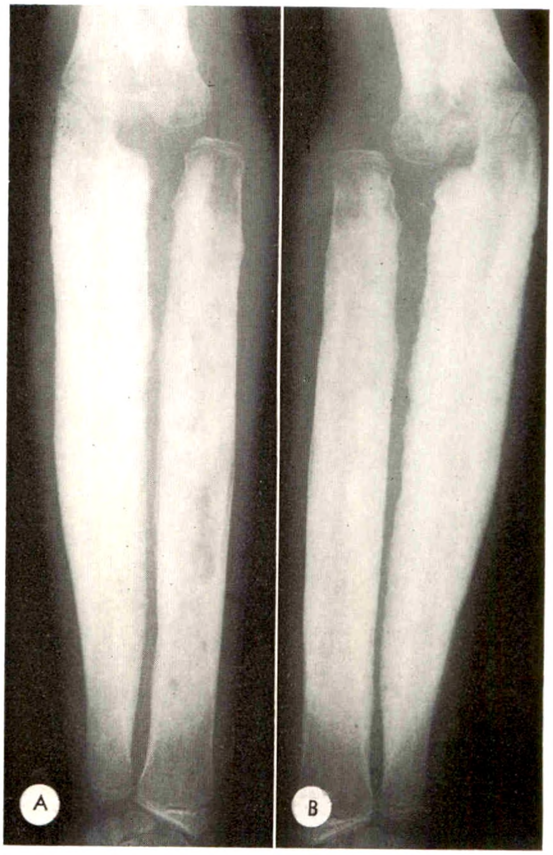

Fig. 8. (*A* and *B*) Aged 12½ years. Note subluxation of radial heads secondary to shaft thickening.

Extremities. The increased width of both bones of the forearms was now such that the radial heads had subluxated laterally. Several of the metacarpals were involved.

FOURTH ROENTGEN EXAMINATION. At the age of 12½ years, she had not developed her secondary sex characteristics nor had she started menstruating. Her weight was 68 pounds and she was 56 inches tall. The weakness and muscle tone remained unchanged. There was intermittent, rather severe, leg pain. There was no papilledema, proptosis or headache. Intelligence was normal.

At this time, the roentgen findings were as follows:

Extremities. Genu valgum was demonstrated

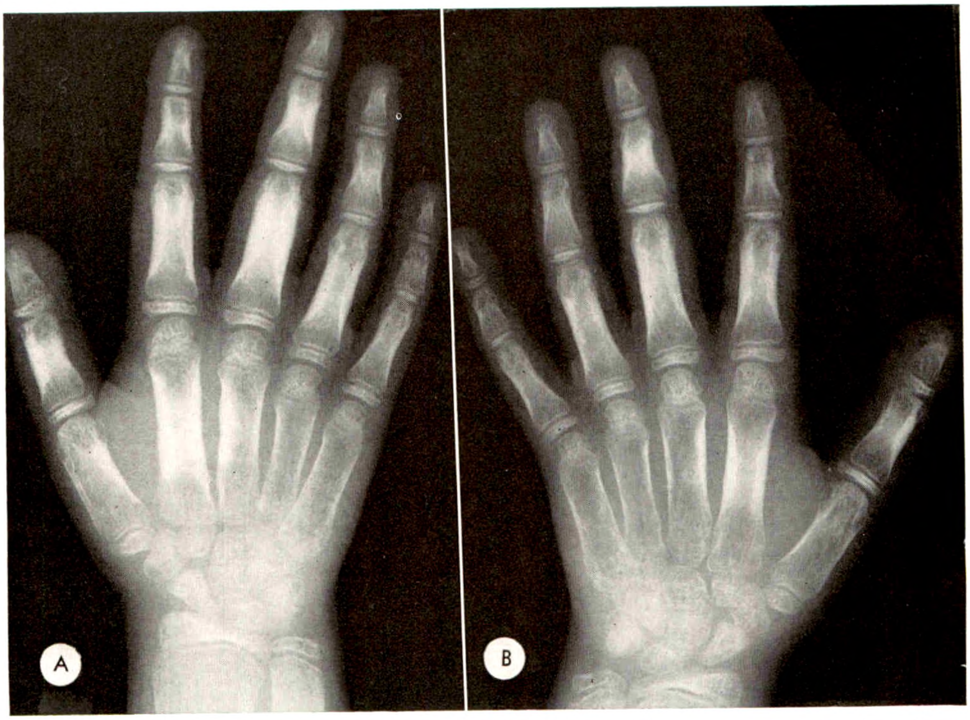

FIG. 9. (*A* and *B*) Aged 12½ years. Almost symmetric involvement in several metacarpals and phalanges.

and even more marked bilateral mottled sclerosis of the shafts of the femora, tibiae and fibulae (Fig. 7). The upper femoral metaphyses showed involvement with some sclerosis in the capital epiphyses.

The subluxation of the radial heads had become more exaggerated and the shafts showed even further thickening, sparing only the metaphyses at the lower ends of the radii and ulnae and the epiphyses (Fig. 8, *A* and *B*). The upper and lower humeral metaphyses showed some involvement. Several phalanges and meta-

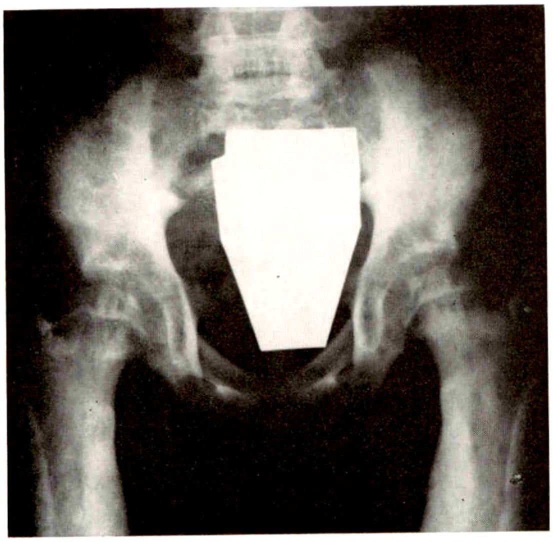

FIG. 10. Aged 12½ years. Pelvic involvement with sclerosis along the iliac sides of the sacroiliac joints, in the femoral epiphyses and metaphyses, and a coarse pattern in the 5th lumbar vertebra.

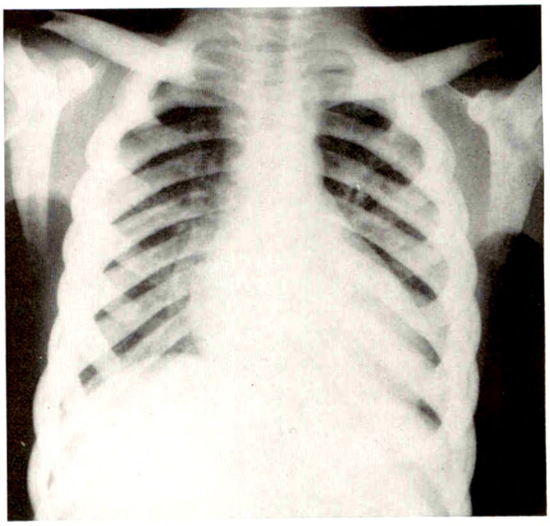

FIG. 11. Aged 12½ years. Note diffuse sclerosis and thickening of ribs, clavicles, and scapulae.

carpals demonstrated sclerosis and thickening of the diaphyses (Fig. 9, *A* and *B*).

Pelvis and Spine. The spine now showed a coarse trabecular pattern in the vertebral bodies and their processes. In many of the bodies a "bone within a bone" pattern was visualized. The pelvis demonstrated mottled sclerosis, mostly along the iliac sides of the sacroiliac joints (Fig. 10).

Skull and Flat Bones. In the skull and flat bones, slight further progression of the sclerosis and thickening was seen (Fig. 11).

At present the child is 14 years of age. She weighs 71 pounds and is 57 inches tall. Her skull circumference is 58 cm. There have been no serious illnesses and there are no residual neurologic findings. Elbow flexion is limited to 25 per cent of normal. The only complaint is leg pain which is not controlled by aspirin. There has been no significant change in her appearance or gait since the last examination.

SUMMARY

A case of diaphyseal dysplasia is reported. Of particular interest were:

1. The extensive skull involvement with increased intracranial pressure.
2. The marked thickening of the radial and ulnar shafts with subluxation of the radial heads.
3. The widespread skeletal involvement, especially in the skull, metacarpals, phalanges, spine and ribs.
4. The relatively rapid progression of the lesions.

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METAPHYSEAL AND PHYSEAL INJURIES IN CHILDREN WITH SPINA BIFIDA AND MENINGOMYELOCELES

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EDWARD B. D. NEUHAUSER, M.D.*

CHILDREN with spina bifida and underlying cord abnormalities, who are not fully paralyzed, are prone to suffer repeated injuries resulting in bizarre skeletal changes at the metaphyseo-physeal junctions of their lower extremities. Seven cases are reported in this paper, 5 from Boston and 2 from Arkansas. The purpose of the authors is to report these cases as a group, as well as to place this entity into a spectrum of metaphyseo-physeal injuries of widely differing pathogenesis.

CLINICAL FEATURES

All these children had major abnormalities of the lumbosacral portion of the spinal cord, its covering membranes and skeleton and had surgical interventions for these spinal abnormalities. Six had meningomyeloceles, 1 had an epidural lipoma.

The common underlying abnormalities resulted in varying degrees of: (1) cutaneous anesthesia of the lower extremities; (2) muscular atrophy secondary to intermittent and long periods of disuse; (3) absence of the deep tendon reflexes due to interruption of the reflex arc in the cord; and (4) complex and varied malformations and joint injuries of the lower extremities, requiring crutches, casts and occasionally corrective surgery. Yet, despite all these handicaps, these children were all "walkers," although all started late and most of them needed orthopedic support. (The clinical details are summarized in Table 1.)

ROENTGENOLOGIC FINDINGS

The osseous changes were best seen in the ankle and knee joints after prolonged weight bearing. Although some of these roentgenograms were quite bizarre, varying degrees and grouping of the following component changes could be recognized on most: (1) irregular, dense, slightly widened metaphyses; (2) widened cartilaginous epiphyseal plates (: physis*); and (3) subperiosteal new bone formation.

The secondary ossification centers (:epiphysis*) were usually intact and secondary demineralization was marked in some cases but completely absent in others. (The roentgenographic changes are summarized, case by case, in the legends of Figures 1 through 10, inclusive.)

DISCUSSION

We believe that trauma is the key factor in the pathogenesis of these complex clinical and roentgenologic findings. The anatomic and physiologic properties of the metaphyseo-physeal junction are pertinent. In this area the periosteum is thick and strongly attached to the physis. Consequently, in case of trauma, metaphyseal infractions are more common than tears of the periosteal fibers.[1] The metaphyseo-physeal junction has limited ways of responding to trauma. If the trauma is sufficiently severe and if the bones are weakened, outright suprametaphyseal fracture or physeal dislocation may occur.[8] Trauma of lesser degree, particularly if repeated, will result in metaphyseal infractions, subperiosteal hemorrhage and perhaps hemorrhage into the physis. Subsequent healing attempts will be manifested by endosteal and periosteal callus formation as well as

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* Nomenclature according to: Rubin, P. Dynamic Classification of Bone Dysplasias. The Year Book Publishers, Inc., Chicago, Ill., 1964.

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Table I

CLINICAL FINDINGS

Case	Birthdate	Diagnosis	Operation	Sensory Changes	Muscle Examination	Reflexes	Started to Walk
1) C.M.	12/24/50	Meningomyeloceles; bilateral clubfeet; incontinence of urine and feces	Meningomyelocele removed at 8 wk. of age	Right: no sensations below the midcalf Left: no sensations below the knees*	Intact thigh muscles; marked atrophy of the muscles below the knees bilaterally	Normal patellar reflexes; absent ankle reflexes bilaterally	At the age 3 yr. with crutches
2) R.W.	4/ 9/41	Meningomyelocele; incontinence of urine and feces	Meningomyelocele and extradural lipoma removed in infancy	Hypoesthesia from L1 to L3 segments; anesthesia from L4 to S3; ulcers on the right foot	Marked atrophy of the muscles below the hips bilaterally	Patellar and ankle reflexes absent bilateraly	On the knees at 2 yr., with braces at 4 yr., without braces at 5 yr. of age
3) D.G.	2/ 7/49	Meningomyelocele; bilateral clubfeet; incontinence of urine and feces	Meningomyelocele removed at 13 mo. of age	Anesthesia from L4 to the S3 segments bilaterally	Marked atrophy of the muscles from the hips down bilaterally	Patellar and ankle reflexes absent bilaterally	At the age of 3 yr. with crutches
4) L.C.	9/22/49	Meningomyelocele; communicating hydrocephalus; dislocated hips; incontinence of urine and feces	Suboccipital decompression of the hydrocephalus; no surgery was done for the meningomyelocele	Anesthesia from L4 to S3 segments; hypoesthesia from L1 to L3 segments	Marked atrophy of the muscles below the hips, more extensive on the left side	Abdominal, patellar and ankle reflexes absent bilaterally	At the age of 3 yr. with crutches
5) D.L.C.	12/30/40	Epidural lipoma at D11–12; incontinence of urine and feces	The lipoma was partially removed and the surrounding adhesions freed	Left: normal Right: anesthesia from L1 to S3 segments; improved after surgery	Left: normal Right: atrophic muscles from the knee down	Left: normal Right: patellar and ankle reflexes absent	No definite information available
6) K.L.	1/13/43	Meningomyelocele; dislocated hips; incontinence of urine and feces	Exploration of the lumbar canal; multiple cauda equina abnormalities found; no corrective surgery done	Hypoesthesia below the hips*	Marked atrophy of the muscles below the hips bilaterally	Patellar reflexes absent bilaterally	At the age of 4 yr.
7) M.C.	5/21/58	Meningomyelocele; dislocated hips; bilateral clubfeet; incontinence of urine and feces	Meningomyelocele removed at 3 mo. of age	Hypoesthesia of the thighs; anesthesia below the knees*	Marked atrophy of the muscles below the hips bilaterally	Patellar and ankle reflexes absent bilaterally	Stood alone with crutches at 2½ yr., walked with crutches at 3 yr. of age

* Exact segmental localization not available.

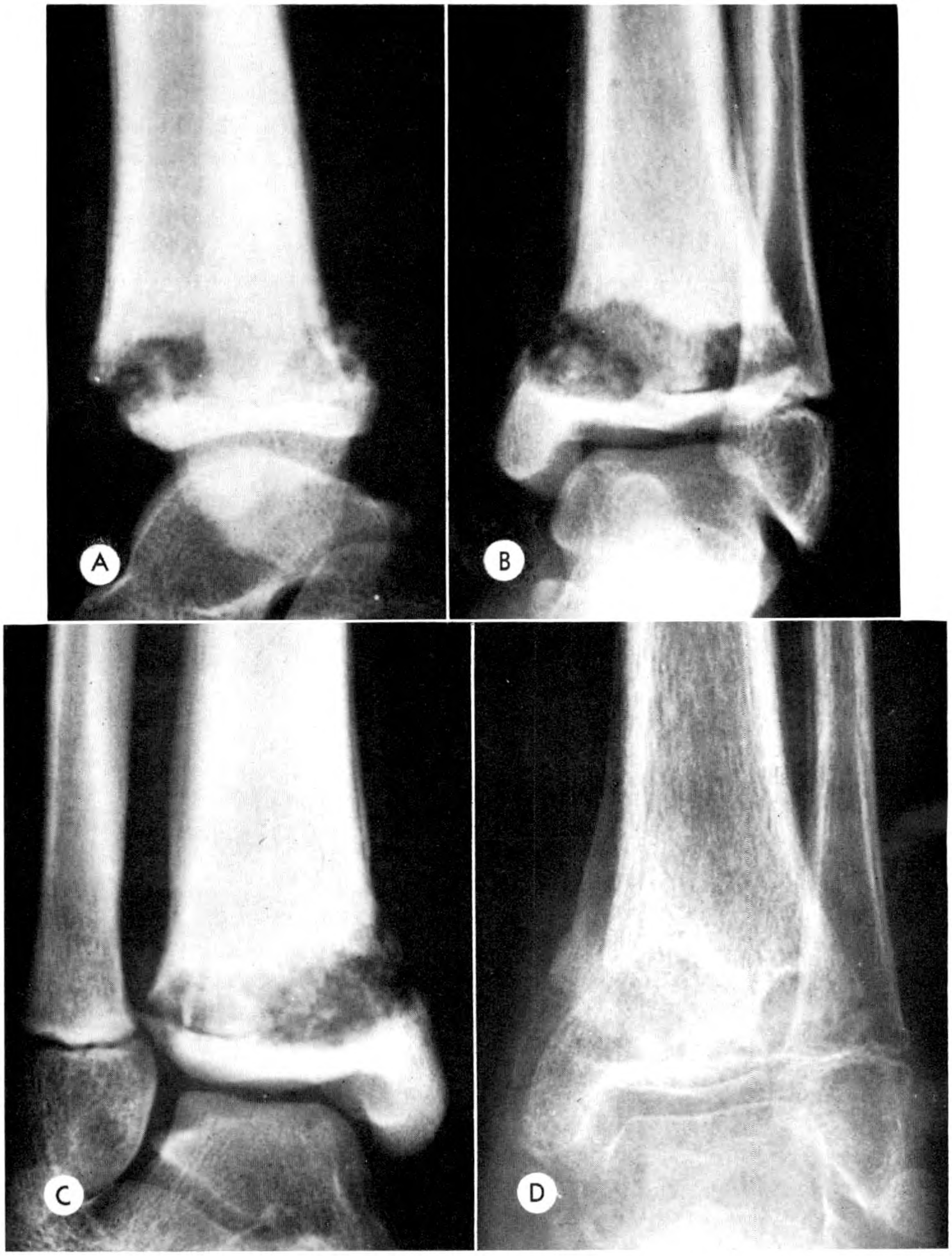

FIG. 1. Case 1, C.M. (*A*, *B* and *C*) Left ankle, 9/3/63. Lateral, oblique and anteroposterior roentgenograms show extensive irregularity of the distal tibial metaphysis with actual disappearance of the zone of provisional calcification. The physis is markedly widened and the epiphysis itself is quite narrow. There is early subperiosteal new bone formation. There is no generalized undermineralization present. (*D*) Left ankle, 12/2/63. The single posteroanterior roentgenogram reveals slight residual widening and irregularity of the metaphysis. There is an attempt seen to reform the zone of provisional calcification. The physis is still narrow. There is more subperiosteal new bone formation seen as well as marked, general undermineralization of all the osseous structures.

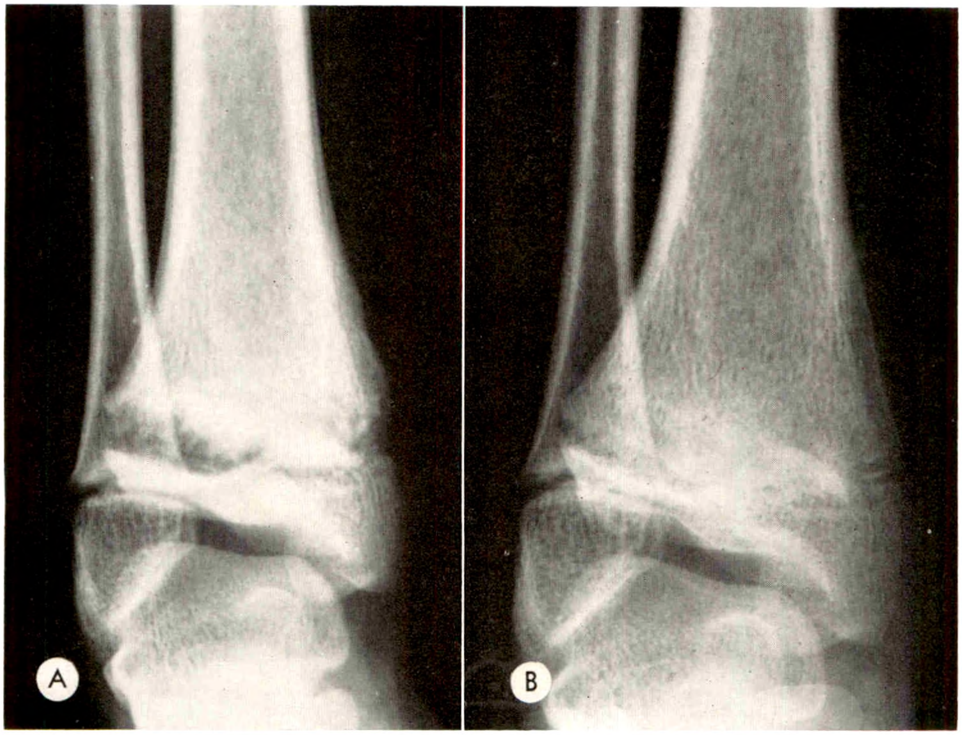

FIG. 2. Case 1, C.M. (*A*) Right ankle, 9/3/63. The distal tibial metaphysis is slightly widened and markedly irregular. The zone of provisional calcification is increased in density. The physis is moderately widened, the epiphysis is somewhat narrowed. There is subperiosteal new bone formation. (*B*) Right ankle, 12/2/63. The metaphysis remains slightly widened but is not irregular any more. The physis is grossly normal now. The medial portion of the zone of provisional calcification remains dense. The epiphysis is still narrow.

by a certain degree of undermineralization due to immobilization.

Muscular paralysis alone, resulting in immobilization and muscular atrophy, will not explain these changes.[9] To re-evaluate this point, the roentgenograms of 50 children with proven poliomyelitis were reviewed. Although from the roentgenologic point of view these cases were selected at random, they represented an even distribution of minimal to severe muscle impairment determined by physical examination and performance tests. In none were any changes similar to those seen in the extremities of children with spina bifida and meningomyeloceles observed.

The fact that these children have varying degrees of insensitivity to pain but nevertheless do walk is very important. A similar entity, "congenital insensitivity to pain" has been recognized as a cause of bizarre skeletal changes and described by Silverman and Gilden,[13] and Fanconi and Ferrazzini,[5] amongst others (Murray, Ford, Wilkins, etc., as cited by Silverman and Gilden[13]). It can be definitely stated that congenital insensitivity to pain leads to a form of juvenile Charcot's joint. The "traumatic theory" is now widely accepted in the explanation of the pathogenesis of Charcot's joint.[3] "Trophic" nerves or the trophic influence of either motor or sensory nerves has never been proven—or disproven—histologically or experimentally, but there is experimental proof available to show that the osseous changes of Charcot's joint can be produced by trauma alone in the insensitive joints.[4,14]

In the few cases where we have good follow-up roentgenograms, it can be seen that the osseous changes in the extremities of these children have not proved to be progressive, in fact these changes rather regressed. The reason for this is that con-

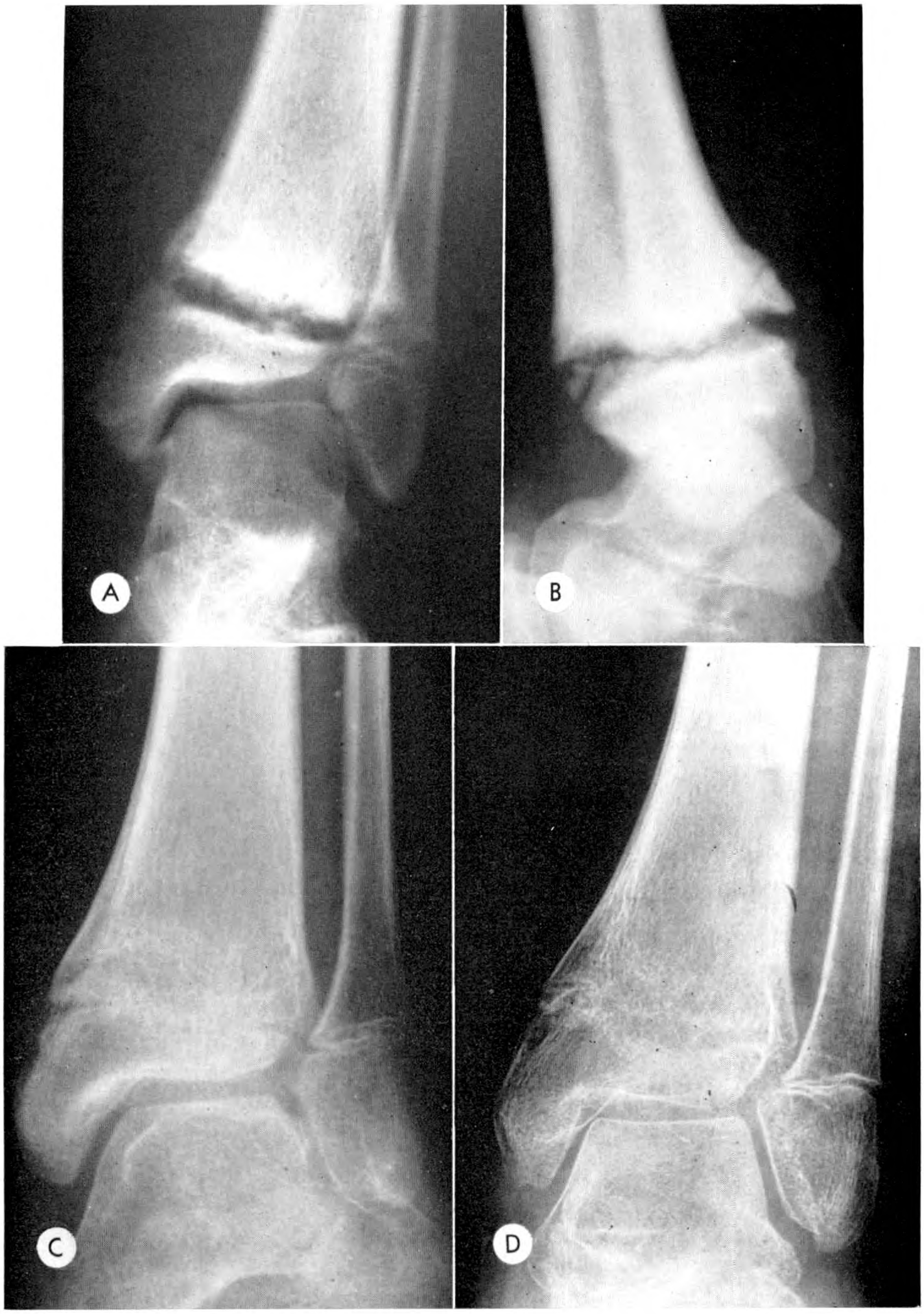

FIG. 3. Case 2, R.W. (*A* and *B*) Left ankle, 10/30/53. The distal tibial metaphysis is slightly widened and irregular. The zone of provisional calcification is considerably increased in density. The physis is slightly widened, there is minimal subperiosteal new bone formation but no generalized undermineralization. (*C*) Left ankle, 5/8/54. The metaphyseal changes disappeared. The physis appears to be closing. There is minimal subperiosteal new bone formation and the bones are slightly undermineralized. (*D*) Left ankle, 4/18/55. The physis has almost fused. The bones are now considerably undermineralized.

tinued weight bearing is a prerequisite for the progression of Charcot's joint and the true late changes of excessive condensation and joint decomposition do not develop in paraplegics.[10] Our patients had long periods of bed rest and immobilization in between periods of walking and thus the late changes could not develop. The actual regression is due to the healing of the fractures themselves and severely damaged bones may return to almost normal on bed rest and immobilization.[2]

The widening of the physis is of interest because it has been reported only rarely in similar cases. The answer, we suspect, lies in the disturbance of the *normal* resorption mechanism of bone development at the metaphysis, probably caused by the metaphyseal infractions.[11] Perhaps the widening of the physis might be due to hemorrhage into the cartilaginous plates themselves. There is histologic evidence to support the above described explanation of the pathogenesis of these osseous changes, although few cases were biopsied. One similar case was biopsied in 1938 and the histologic report was "abundant callus."[7] One of Fanconi and Ferrazzini's cases of congenital insensitivity to pain was biopsied; the histologic report was callus again. Case 1 in our series was biopsied but the biopsy did not reach deep enough into the physis. However, 2 cases reported by Soutter[15] in 1962 were very well documented. The clinical histories and roentgenograms leave no doubt that Soutter's cases are identical

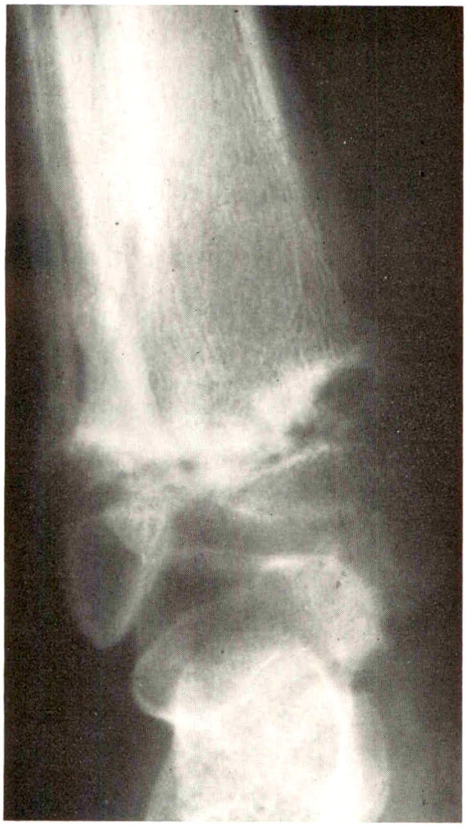

Fig. 4. Case 2, R.W. Right ankle, 10/3/53. The distal tibial metaphysis is widened and markedly irregular. The density of the zone of provisional calcification is increased. The physis is slightly widened and there is considerable subperiosteal new bone formation. The epiphysis is normal.

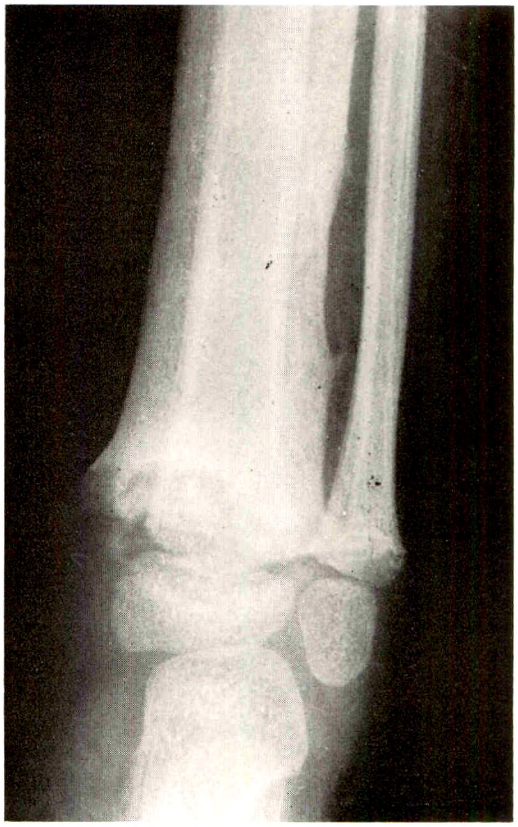

Fig. 5. Case 3, D.G. Left ankle, 12/15/52. The distal tibial metaphysis is moderately irregular. The normal density of the zone of provisional calcification is decreased. The epiphysis and the physis are normal. There is extensive subperiosteal new bone formation.

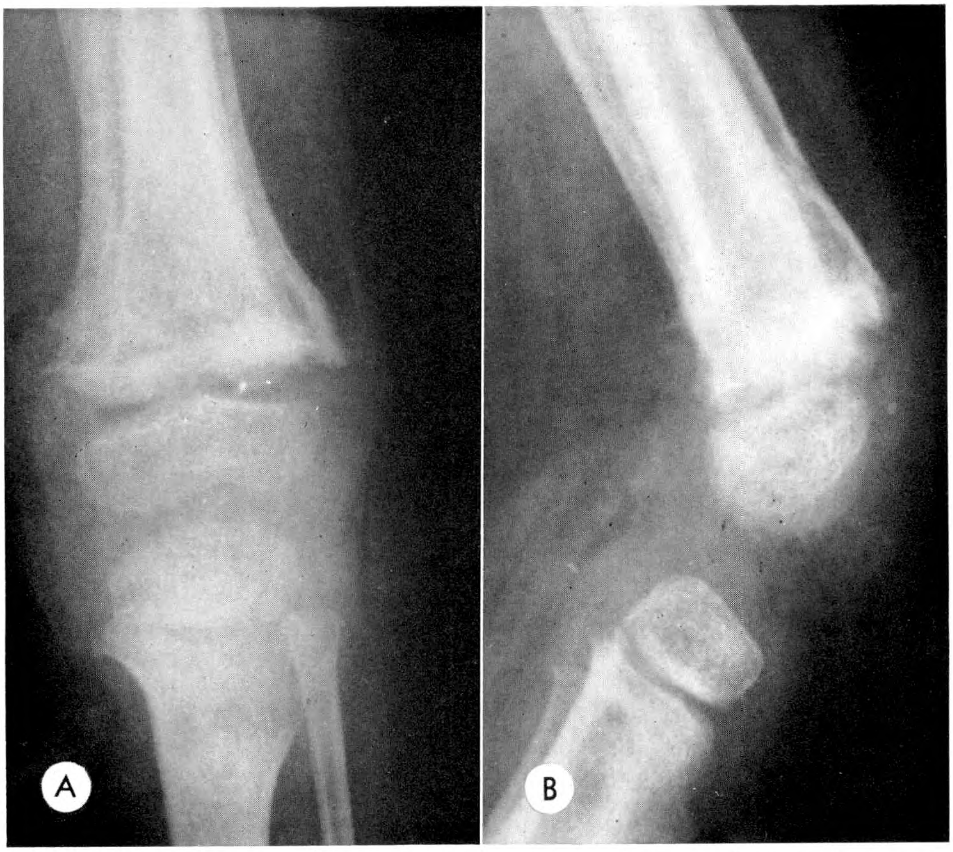

FIG. 6. Case 4, L.C. (*A* and *B*) Left knee, 2/8/53. The distal femoral metaphysis is widened and slightly irregular. The density of the zone of provisional calcification is increased. The physis is slightly widened. The epiphysis is normal. There is extensive subperiosteal new bone formation present. The bones are not undermineralized.

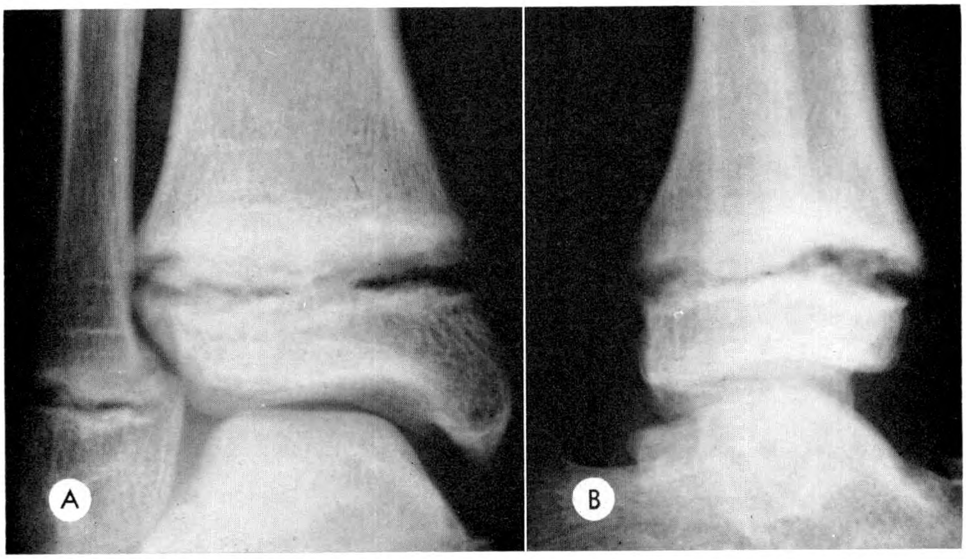

FIG. 7. Case 5, D.L.C. (*A* and *B*) Right ankle, 11/17/52. The distal tibial metaphysis is slightly widened and moderately irregular. The density of the zone of provisional calcification is increased. The physis is slightly widened and the epiphysis is normal. There is no subperiosteal new bone formation seen and the bones are not undermineralized.

to ours and represent the same entity. The metaphyseo-physeal junctions were successfully biopsied in his cases and the sections showed "fragments of normal living bone. The marrow space was occupied by delicate connective tissue and a small amount of resolving granulation tissue"—in other words, callus and evidence of healing fractures.

The roentgenologic changes thus become clearly understandable—if one considers them as illustrations of the pathologic process, at a given point in the evolution of the process. No single film tells the "whole story" and the illustrations differ from each other not only because they were taken at different stages of the same process but also because they represent cases of varying severity within the same entity.

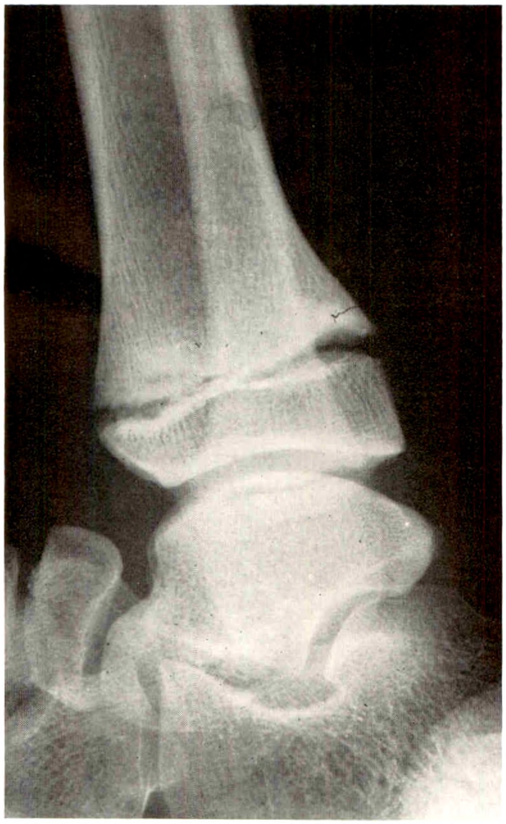

FIG. 8. Case 6, K.L. Right ankle, 7/23/54. The distal tibial metaphysis is slightly widened and irregular. The zone of provisional calcification is within normal limits. The physis and the epiphysis are normal. There is no subperiosteal new bone formation. The bones are not undermineralized.

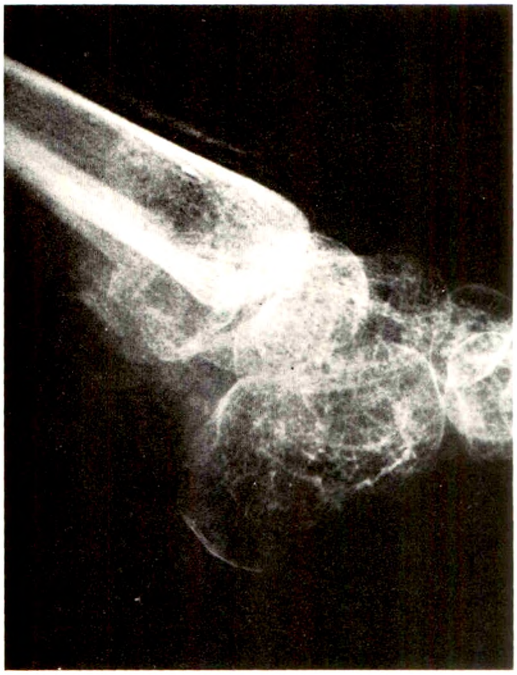

FIG. 9. Case 7, M.C. Right ankle, 11/5/63. The distal tibial metaphysis is not irregular or widened. The physis is not widened. There is a suprametaphyseal fracture through the distal fibula with moderate callus formation. All the bones are extensively undermineralized.

There seem to be a number of entities in which the roentgenologic findings are very similar and, clinically, in all of them there are predisposing factors facilitating the occurrence and repetition of trauma. Since, regardless of etiology, the "response" of the metaphyseo-physeal junction to trauma will be the same, with quantitative variations only, these entities form a spectrum from severe to minimal osseous changes. At the one end of the spectrum we find the bedridden paraplegic whose osteoporotic bones may snap, usually at the time of handling, and suprametaphyseal fractures result. In scurvy, it is the poor quality of the bone matrix which leads to infractions and subperiosteal hemorrhage upon exposure to normal wear and tear. In children with spina bifida and meningomyeloceles, congenital and perhaps unavoidable iatrogenic causes play their

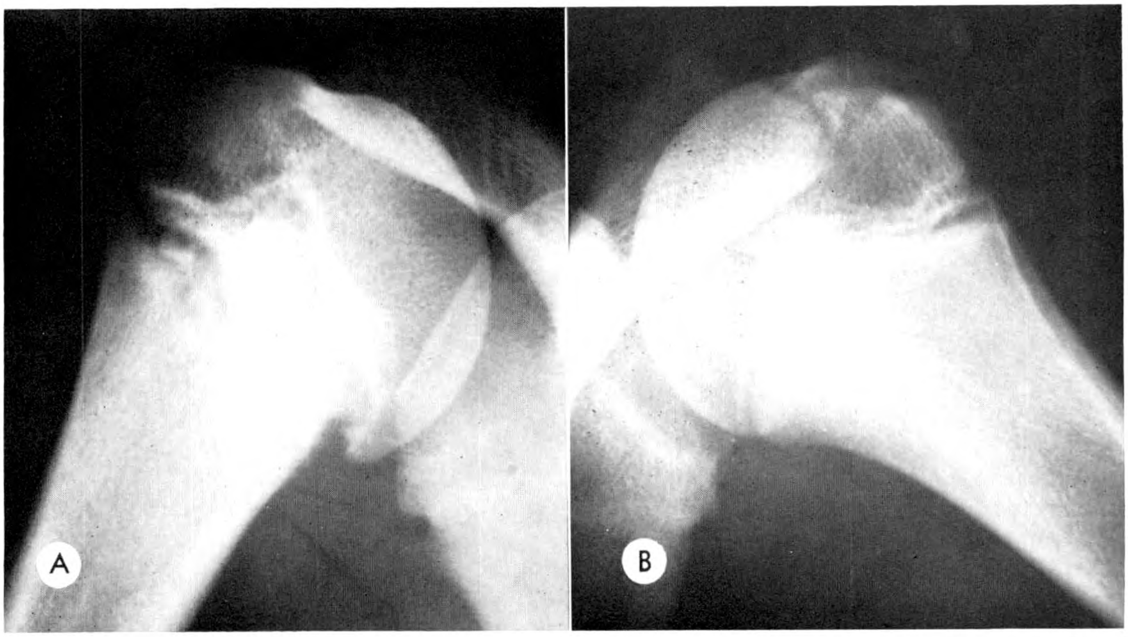

FIG. 10. R.A. (*A*) Right shoulder. The proximal humeral metaphysis is irregular and the normal density of the zone of provisional calcification is increased. The physis is slightly widened; the epiphysis is normal. There is no subperiosteal new bone formation and the bones are not undermineralized. (*B*) Left shoulder. Completely normal osseous structures.

parts in rendering joints insensitive and "oblivious" to the pain of trauma. The similarities between these osseous changes and those of congenital insensitivity to pain have already been mentioned, although the exact etiology of the latter entity is still unexplained. In so-called "unrecognized trauma,"[12] particularly in battered children, it is the abnormal exaggeration and repetitiveness of trauma itself which cause the same results. Fractures associated with chronic subdural hematoma in children and metaphyseal fragility are probably also due to unrecognized trauma. We have not yet seen but expect to encounter similar changes in children with the Riley-Day syndrome, as these children also suffer from insensitivity to pain. At the other end of the spectrum, a good case may be made for considering slipped capital femoral epiphysis similar and related to these above described entities. Slipped capital femoral epiphysis usually occurs in overweight teenagers and the actual slip is not a true dislocation but rather a separation through the metaphysis.[6] The roentgenologic changes at the metaphyseo-physeal junction are identical with some of the above illustrated changes seen in the extremities of children with spina bifida, congenital insensitivity to pain and other entities in this spectrum. Without wishing to minimize the complexity of biochemical and anatomic factors, it seems quite plausible to us that slipped capital femoral epiphysis, as an entity, represents the end result of continuous excessive stress on the proximal metaphyseo-physeal junction of femur, caused by relative overweight and facilitated by thus far unknown factors.

Finally, we have recently seen a boy who repeatedly injured his shoulder playing baseball (pitching) but continued to play through the rest of the season despite moderate pain. The roentgenologic changes (Fig. 10*A*) were extremely similar to those seen in congenital or acquired insensitivity to pain, or, for that matter, to the metaphyseal changes in slipped capital femoral epiphysis. This "psychologic" insensitivity to pain is a rare but revealing constellation of circumstances further supporting the above outlined explanation of the pathogenesis of osseous changes in these entities.

SUMMARY

Bizarre skeletal changes are frequently seen in the lower extremities of children with spina bifida vera and meningomyeloceles who are not completely paralyzed. These changes are due to multiple small fractures and subsequent healing at the metaphyseo-physeal junctions in insensitive extremities, which are subjected to the chronic stress of weightbearing. There are a number of entities in which the underlying pathology is identical: repeated trauma—but the predisposing factors to trauma are multiple and varied. These different entities form a spectrum of metaphyseo-physeal injuries. The spectrum extends from the gross abnormalities of bedridden paraplegics, through severe changes in children with insensitivity to pain of differing etiology to the least pronounced metaphyseal changes in slipped capital femoral epiphysis.

It is hoped that the recognition of these skeletal changes and the understanding of their pathogenesis will prevent the needless surgery of open biopsy or aspiration for culture to which many of these children were subjected in the past.

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DYSCHONDROSTEOSIS, A HEREDITABLE BONE DYSPLASIA WITH CHARACTERISTIC ROENTGENOGRAPHIC FEATURES

By LEONARD O. LANGER, Jr., M.D.
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DYSCHONDROSTEOSIS, a hereditable bone dysplasia, was first described by Léri and Weill[14] in 1929 in the French literature, and since that time, occasional reports have appeared in the French,[10,14,16] German[4] and Spanish literature.[6] A French case with this condition is illustrated in Rubin's Dynamic Classification of Bone Dysplasias.[17] The diagnosis of this process rests on the roentgenographic findings. Seven affected individuals in 3 families have been studied at the University of Minnesota Hospitals during the last 3 years. Roentgenographic studies in 4 other individuals with the typical wrist deformity were found in the files of the radiology department in the course of reviewing roentgenograms of bone dysplasia and in routine work. These latter individuals were not available for study and are not included in this report.

The first 2 families in this report are described in a clinical paper to be published by Herdman, Langer, and Good[8] and, to my knowledge, excepting the present study, are the only cases reported under the term of dyschondrosteosis in the English literature, including the first documented case in a male. However, cases with the characteristic wrist deformity of dyschondrosteosis have been reported in the past under the name of Madelung's disease.

The purpose of the author is: (1) to describe the roentgenographic features of dyschondrosteosis, emphasizing the wide spectrum of manifestations, (2) to show that, according to the experience at the University of Minnesota Hospitals, dyschondrosteosis and Madelung's disease are the same condition and that the distinctions which have been made between them are not valid, and (3) to suggest that "Madelung's deformity" be used as a descriptive term for the characteristic wrist deformity, regardless of etiology.

Dyschondrosteosis has an autosomal dominant mode of genetic transmission. All previously reported bona fide cases have been found in females, although several of the authors have mentioned unexamined apparently affected male siblings.

Briefly, the clinical features of dyschondrosteosis are as follows:

1. Shortening of the forearm in respect to the upper arm and hand.
2. Dorsal dislocation of the distal ulna which is easily reducible but which cannot be maintained in position. This wrist deformity has been referred to as Madelung's deformity.
3. Limitation of motion at the elbow and wrist.
4. Shortening of the shank in relation to the upper leg, which results in mild dwarfism. This pattern of shortening in the middle segment of the extremities is referred to as mesomelia.

The most prominent abnormality of dyschondrosteosis is in the wrist. Dannenberg, Anton and Spiegel[5] outlined 12 roentgenographic criteria for the diagnosis of Madelung's deformity. Their criteria, based on 2 personal cases and 170 cases reported in the world literature, are as follows:

1. A double (lateral and dorsal) bowing of the radius which involves the entire diaphysis but is most marked at the distal end. This is best seen on roentgenograms obtained with the hand in pronation.
2. A variable widening of the interosseous space due to the lateral curvature described above.
3. Shortening of the radius as compared

with the normal standard for age and in relationship to the size of the other bones of the upper extremity.

4. An alternation of the contour of the distal radius so that the articular surface of the epiphysis faces in an ulnar and palmar direction.

5. Premature fusion in the ulnar half of the epiphyseal line of the distal radius which contributes to accentuation of the deformity in early adolescence.

6. Dislocation or subluxation of the inferior radio-ulnar articulation with the distal ulna dorsal to the distal radius.

7. An area of decreased bone density on the ulnar border of the radius extending for a short distance proximal to the fused epiphyseal line.

8. Small bony excrescences, sometimes condensed into an exostosis along the inferior ulnar border of the radius.

9. Triangularization of the normally quadrangular shaped outline of the distal radial epiphysis, with the apex of the triangle pointing medially.

10. Hypercondensation of trabeculations of the ulnar head.

11. A change in the inferior radial articular surface with modification of the relationship of the carpal bones, wedging them between the deformed radius and protruding ulna and giving them a triangular configuration with the lunate at the apex.

12. An arched curvature of the carpal bones, which is a continuation of the arch of the dorsal bowing of the radial diaphysis (Fig. 3 through 5, inclusive).

Analysis of these criteria shows that criteria 3, 9 and 11 are fundamental to the establishment of the diagnosis of Madelung's deformity. Criteria 4, 6, and 12, although present in these patients, may be obscured in mild cases by the failure to obtain a true lateral projection of the wrist. Criteria 1 and 2 are best, and sometimes only, appreciated on roentgenograms of the forearm with the hand in pronation, rather than in the routinely used view with the hand in supination. Criterion 5 is dependent on the age of the patient and is applicable only in the early adolescent period. Criteria 7, 8, and 10 are clearly secondary phenomena and have been recorded by Dannenberg, Anton and Spiegel as less consistent components of the picture. Hypoplasia and flattening of the radial head have also been described.[13]

Other roentgenographic features which are not part of Madelung's deformity but which have been present in some severely affected individuals with dyschondrosteosis are: thickening of the long bones,[3] abnormalities of the anatomic neck of the humerus,[13] exostosis of the proximal medial tibia,[14] shortening and thickening of the metacarpals and phalanges,[3] coxa valga[15] and cubitus valgus.[10] The skull, spine and pelvis have been roentgenographically normal in all cases in which these bones have been studied.

REPORT OF CASES

Case i. R.C., an 11 year old Mexican girl, had been in good health all of her life. A roentgenogram, made to rule out fracture subsequent to trauma, demonstrated the changes of dyschondrosteosis. Subsequent physical examination showed the typical clinical deformities. Her mother stated that the deformity of both wrists had been present since birth and was asymptomatic. Roentgenographic findings in the right forearm met all the criteria for Madelung's deformity outlined by Dannenberg *et al.* with the exception of criterion 10, that is, hypercondensation of trabeculations in the ulnar head. On the left, the changes were not as marked, but it was felt that the criteria fundamental to the diagnosis were present. Of the less frequent findings reported in dyschondrosteosis, only relative hypoplasia of the capital humeral epiphyses and coxa valga were present (Fig. 1; and 4, *A* and *B*) (Table 1).

Case ii. C.C., mother of R.C., also showed the typical deformity of both wrists with reducible dorsal dislocation of the ulna and mesomelia. The deformity was asymptomatic and had always been present. The father had died but was reportedly normal. The 6 siblings of R.C. were said to be normal. Two brothers were examined roentgenographically and showed none of the changes of dyschondrosteosis. The wrists of 3 other siblings were examined clinically and were normal. Subsequent experience has suggested the probable inadequacy of this clinical evaluation (see Discussion). All the criteria for the diagnosis of Madelung's deformity were present in this patient but the changes were mild. The area of decreased bone density on the ulnar border of the radial metaphysis (criterion 7) was exceedingly small, and hypercondensation of trabeculations of the ulnar head (criterion 10) was not present. Criterion 5 could not be applied because the epiphyseal plate was fused. The changes were equal in both forearms. As regards the inconstant abnormalities in other bones reported in dyschondrosteosis, there was the type of change which Kaplan, Guy and Cantagrel[10] described as an exostosis of the medial aspect of the proximal tibial metaphysis. This change was mild and while it was as pronounced as in one of Kaplan and coworkers' patients, it is doubtful that it repre-

TABLE I

Case		I	II	III	IV	V	VI	VII
Clinical Measurements								
Height		129	147	150	145	168	135	144
Arm span		125	148	145	133	159	131	137.5
Lower segment		65	73	71	68.5	79	66	71
Roentgenographic Measurements (Six ft. film target distance)								
Humerus	L	24.6	NE	28.8	23.2	30.5	24.2	25.7
	R	23.8	31.0	28.7	23.5	30.7	24.2	25.0
Radius	L	16.3	NE	16.5	17.2	21.4	16.4	18.2
	R	15.7	20.9	19.2	17.3	21.8	16.6	18.1
Ulna	L	18.2	NE	19.2	19.7	23.1	17.9	20.1
	R	18.0	23.1	21.2	19.3	23.3	18.0	19.7
Hand	L	14.8	16.8	17.1	17.7	19.7	16.9	17.9
	R	14.7	16.8	17.1	17.7	19.5	16.9	17.7
Ratio radius/humerus	L	66%	NE	57%	74%	70%	68%	71%
	R	66%	67%	67%	74%	71%	69%	72%
Normal ratio radius/humerus		74%	74%	75%	74%	76%	75%	74%
Femur	L	38.2	45.7	44.0	41.2	46.9	39.7	39.9
	R	38.4	45.7	44.0	41.0	47.1	39.6	39.7
Tibia	L	29.0	35.0	32.0	31.1	35.5	29.5	29.5
	R	29.2	34.9	32.8	30.8	35.4	29.4	29.6
Ratio tibia/femur	L	76%	77%	73%	76%	76%	74%	74%
	R	76%	76%	73%	75%	75%	75%	75%
Normal ratio tibia/femur	L R	85%	83%	83%	83%	85%	83%	83%

All measurements in cm.
NE = not evaluated.

sents a true exostosis. A mild cubitus valgus deformity was present bilaterally (Fig. 1; 2*B;* and 3*E*) (Table I).

Case III. Ma.H., a 13 year old girl of Northern European extraction, was seen on referral for deformity of the left forearm. The parents and child stated that the deformity had been noted for about 2 years with some gradual progression and that it was asymptomatic. Physical examination showed marked typical changes of dyschondrosteosis in the left forearm and mesomelia of all 4 extremities. The right arm had less marked but definite clinical findings of dyschondrosteosis with dorsal dislocation of the distal ulna. Roentgenographic study showed that the left forearm was much more severely affected than the right. All of the criteria except criterion 10 were present in marked degree on the left. In contrast, on the right only very slight changes were noted (Fig. 2*A;* 3*A;* 4, *C* and *D;* and 5*A*) (Table I).

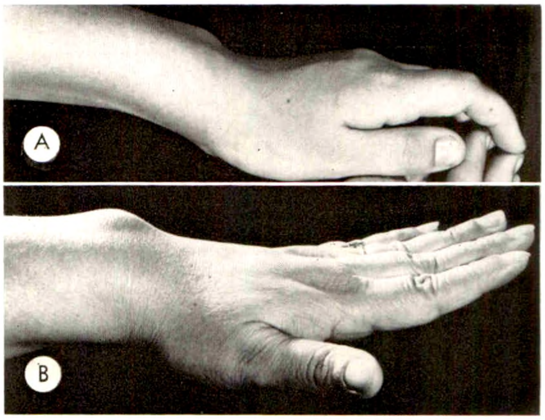

Fig. 2. Clinical wrist deformity. (*A*) Case III. (*B*) Case II.

Case IV. My.H., the mother of Ma.H., showed none of the clinical changes of dyschondrosteosis except shortening of all extremities and mesomelia of the lower extremities. There was no dorsal dislocation of the distal ulna in either wrist. Roentgenographic study showed marked changes of dyschondrosteosis bilaterally in the wrists except that there was no dorsal displacement of the ulnar heads. There was marked osteophyte formation in addition to hypercondensation of trabeculation in the ulnar heads (criterion 10). Findings in other bones included dorsal angulation of the proximal humeri with shortening of these bones, hypoplasia of the humeral heads and bilateral cubitus valgus deformity. A moderate kyphosis of the thoracic spine with secondary osteospondylotic spurring was present (Fig. 3*B;* and 6, *A* and *B*) (Table I).

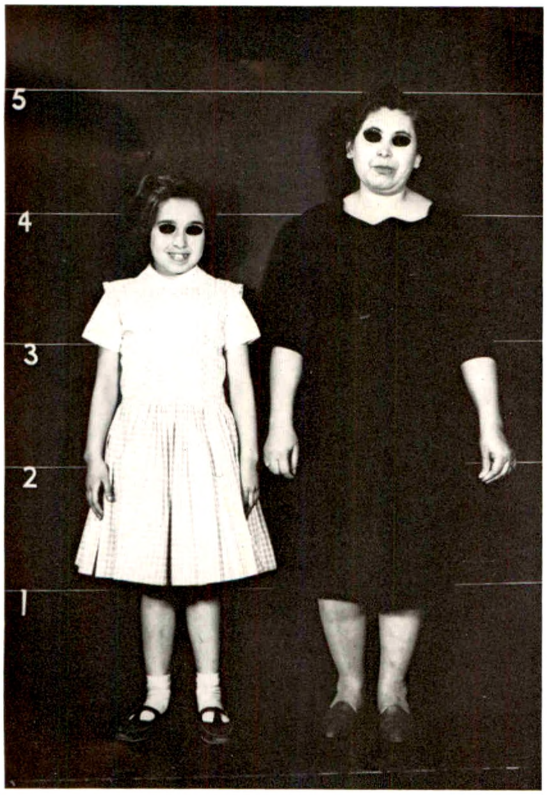

Fig. 1. Case I and II. Note the obvious clinical deformity in wrists of Case I.

Case V. Me.H., the 15 year old brother of Ma.H., was seen by request when his parents reported his comparatively short stature. On physical examination, no abnormalities were noted save mesomelia. Another male sibling, aged 19 years, and a female sibling, aged 9 years, were not seen. They were said to be tall and long limbed like the father, a normal 183 cm. male. Roentgenographic study showed the changes of dyschondrosteosis to be mild and symmetric in both wrists. Symmetric mesomelia of both the upper and lower extremities was present (Fig. 3*F;* and 5*B*) (Table I).

Case VI. M.L., a 13 year old boy of Northern European extraction, was seen in the outpatient clinic because of a cardiac murmur in the aortic region. Further investigation suggested that this was rheumatic in origin and not of functional importance at the present time. Roentgenograms of the hands were obtained to exclude the possibility of Marfan's syndrome. On recall at the request of the radiology department, the patient was found to have the typical clinical findings of dyschondrosteosis in the wrists. Mild mesomelia of all extremities was present. Roentgenographic study showed moderate symmetric changes of dyschondrosteosis in both forearms and wrists. There was no hypercondensation of trabeculations in the ulnar head (criterion 10). There was relative shortening of both 4th metacarpals and prominence of the medial portion of the proximal tibial metaphyses (Fig. 3*C;* and 7*A*) (Table I).

Case vii. D.L., the mother of M.L., was examined at the request of the radiology department. Physical examination showed the same findings as in her son. In addition, the pa-

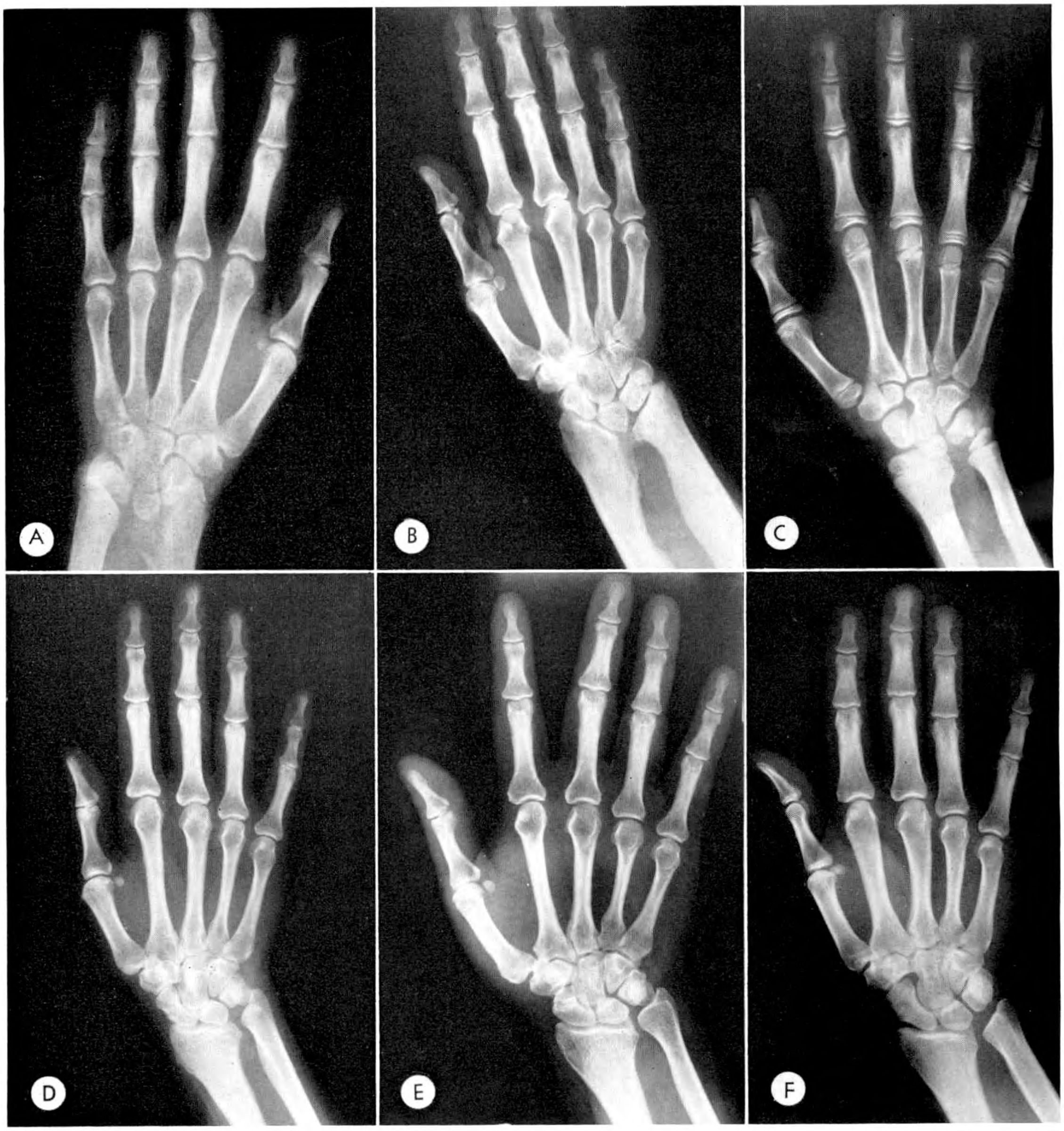

Fig. 3. Roentgenographic wrist deformity. Marked deformity: (*A*) Case iii. (*B*) Case iv. Moderate deformity: (*C*) Case vi. (*D*) Case vii. Mild deformity: (*E*) Case ii. (*F*) Case v.

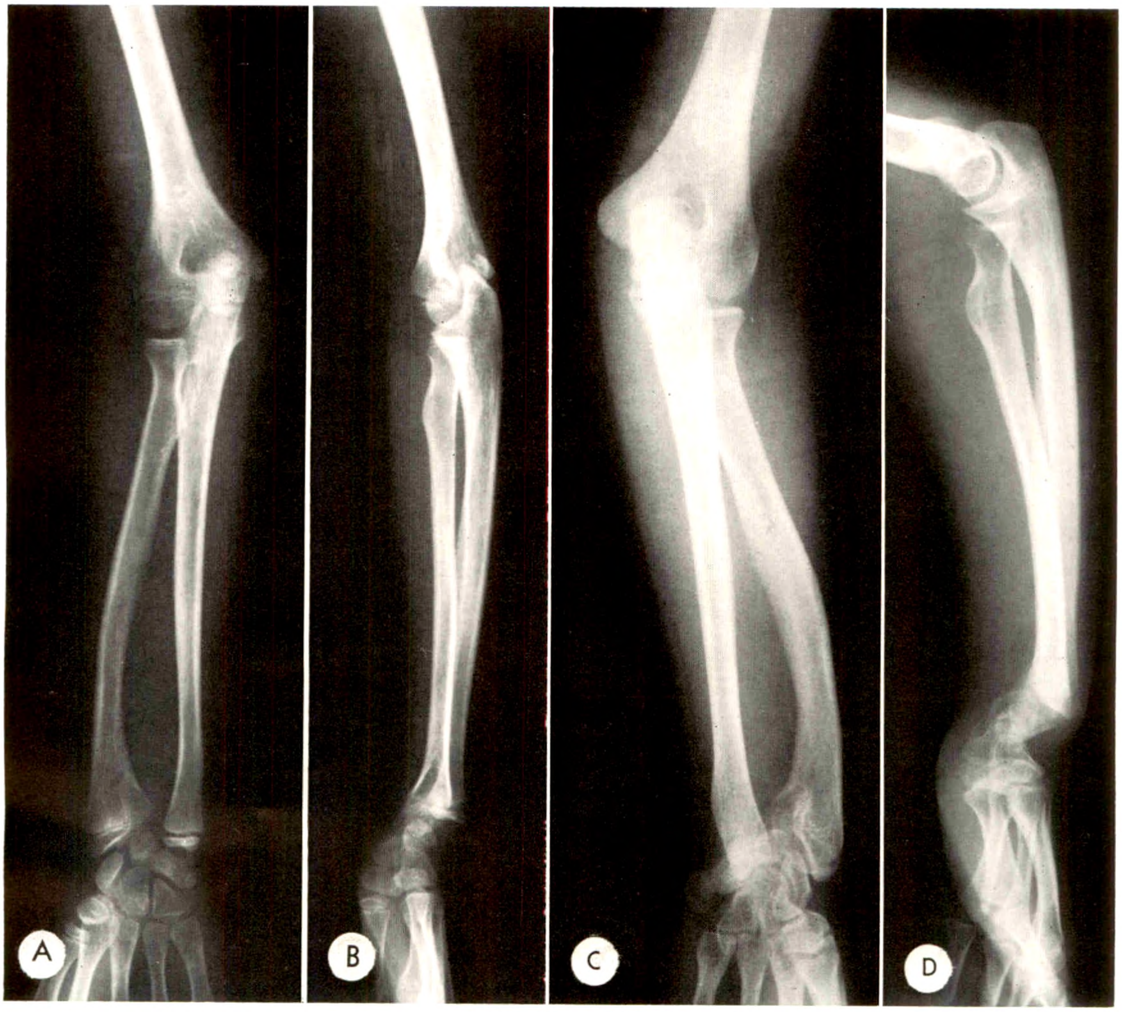

FIG. 4. Typical forearm and wrist deformity (studies in supination). Moderate deformity: (*A* and *B*) Case I. Marked deformity: (*C* and *D*) Case III.

tient had an S-shaped scoliosis of the thoracolumbar spine. Roentgenographic study showed moderate symmetric changes of dyschondrosteosis in both forearms and wrists. Hypercondensation of trabeculations of the ulnar head (criterion 10) was not present. The area of decreased bone density on the ulnar border of the radius (criterion 7) was very small. Other changes included minimal alteration of the surgical neck of the proximal humerus bilaterally and mild genu varum with prominence of the medial aspect of the proximal tibiae. A moderate, apparently idiopathic kyphoscoliosis of the thoracolumbar spine was present (Fig. 3*D*; and 7*B*) (Table I).

ROENTGENOGRAPHIC DIFFERENTIAL DIAGNOSIS

The differential diagnosis should include other conditions causing deformities of the distal forearm. Closely simulating the deformity of dyschondrosteosis is post-traumatic fusion of the ulnar aspect of the distal radial epiphysis. In most instances, the history of trauma to the area can be obtained. Less commonly, infection may result in a similar deformity. The deformity is almost always unilateral in these cases. As shown in the present case reports and

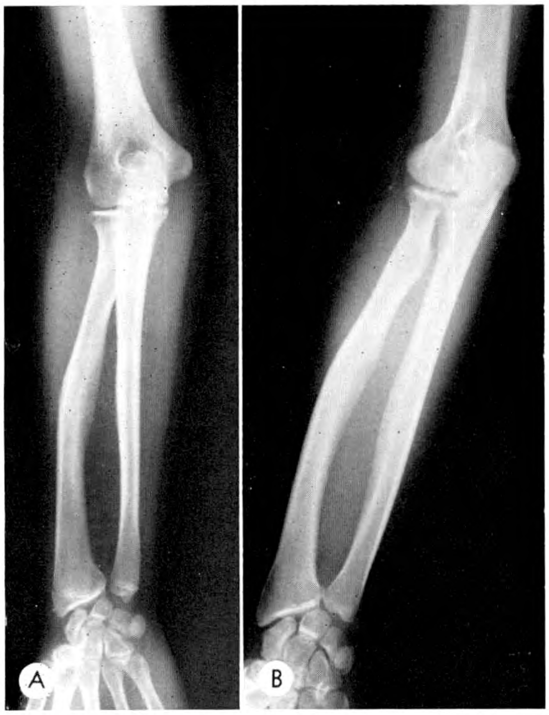

Fig. 5. Most mild forearm deformities of 7 cases studied (studies in supination). (*A*) Case iii. Slight involvement in forearm. Clinical wrist deformity present. (*B*) Case v. Slight changes. No clinical wrist deformity present.

other published cases, dyschondrosteosis may be asymmetric as regards severity of involvement, but invariably, the criteria of dyschondrosteosis are present roentgenographically, if not clinically, in both wrist regions.

A number of generalized dysplasias may present a similar clinical deformity in the distal forearm associated with shortening of this segment. Shortening of the distal radius and ulna is commonly present in hereditary multiple exostoses and in enchondromatosis (Ollier's disease). The wrist deformity is due primarily to a more marked shortening of the ulna with a secondary curvature of the radius, in distinction to the relatively shorter radius present in dyschondrosteosis. Both of these conditions are generalized dysplasias in which roentgenograms of other areas easily establish the correct diagnosis.

Multiple epiphyseal dysplasia of the

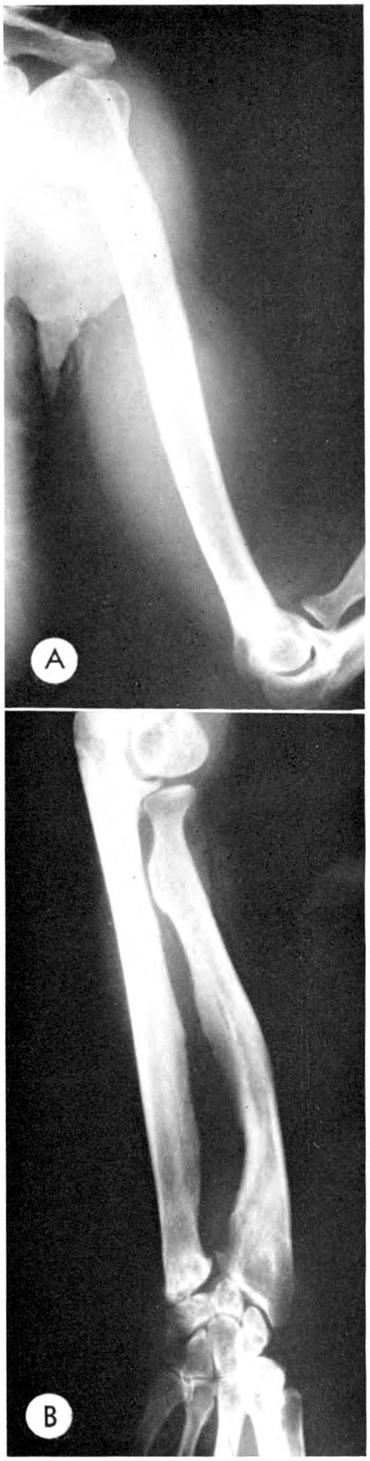

Fig. 6. Case iv. (*A*) Short humerus with dorsal angulation of surgical neck and flattened hypoplastic radial head. (*B*) Marked curvature and irregularity of radial shaft and marked changes in distal radius and ulna (study in supination).

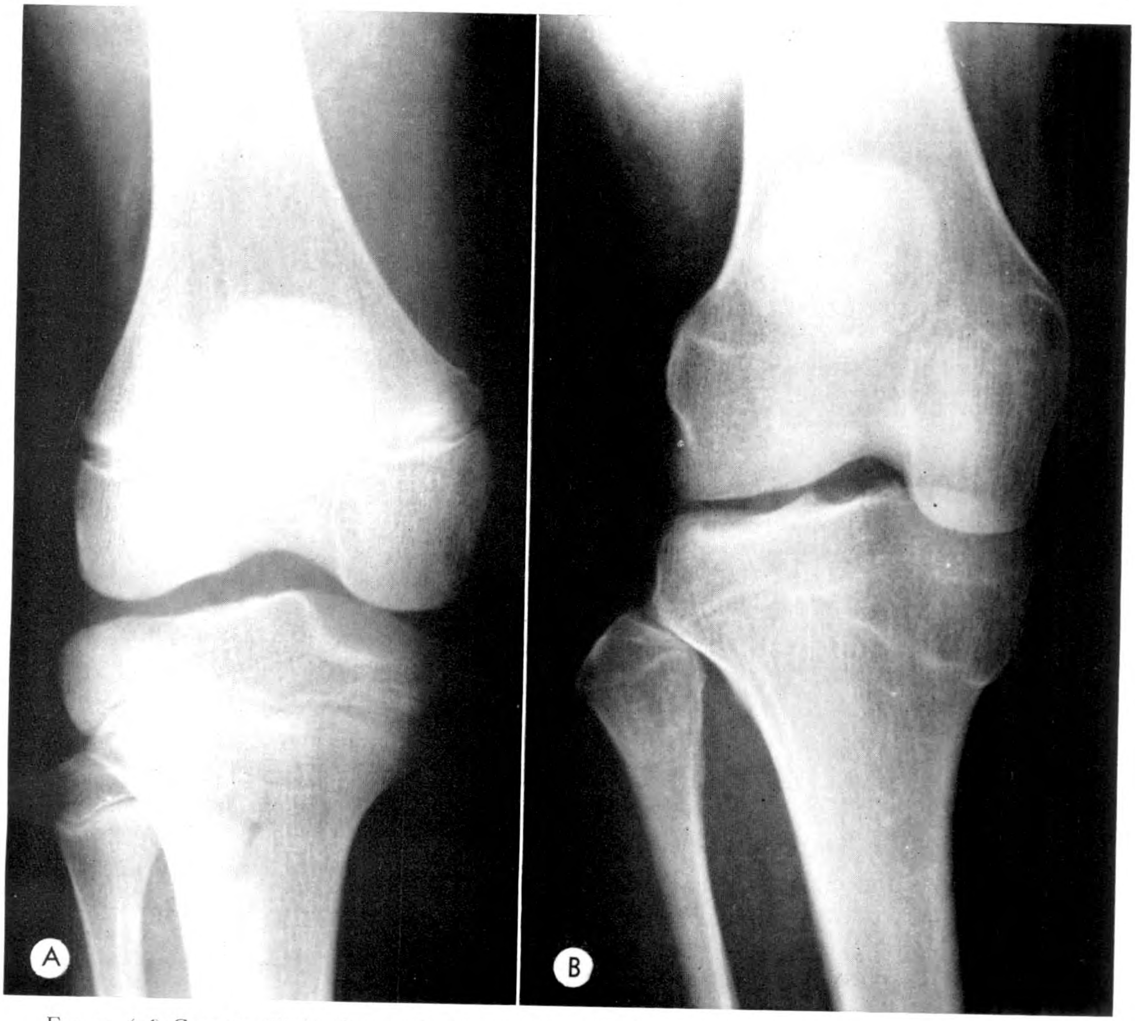

FIG. 7. (*A*) Case VI. Slight changes in knee region. (*B*) Case VII. Moderate changes in knee region.

short limbed variety may lead to dwarfism of the mesomelic type and may show features in the forearm similar to, and in some instances indistinguishable from, those of dyschondrosteosis. However, a roentgenographic skeletal survey reveals generalized involvement of the epiphyses, which is not present in dyschondrosteosis.

In the literature it appears that several cases with bone changes very similar to those seen in mild thalidomide embryopathy have been confused with dyschondrosteosis.[12] In these cases, the mesomelic shortening is in excess of that seen in dyschondrosteosis, and there may be absence of the radius and fibula, which does not occur in dyschondrosteosis.

Case reports of syndromes which probably are not dyschondrosteosis, but with insufficient information have appeared occasionally.[2,9,11] If the roentgenographic criteria for the diagnosis are adhered to, confusion with any of the above entities is unlikely.

DISCUSSION

In the first family, the affected child (Case I) is relatively smaller than her siblings including a 7 year old sister. She has definite mesomelia but does not have a disproportionately short total extremity length. Case II, her mother, who is also short, likewise does not have shortening of the arm span or of the lower segment on clinical examination. These individuals, however, have bilateral clinical and roentgenographic changes of Madelung's deformity which together with the mesomelia and the presence of the wrist deformity since infancy confirm the diagnosis of dyschondrosteosis. It is apparent on the basis of the findings in Cases IV and V that the typical wrist deformity may not be present in dyschondrosteosis and it is impossible, therefore, to be certain that the 3 siblings of Case I, who were examined briefly for this finding, are in fact normal.

In the second family, the 13 year old girl with the marked deformity of the left wrist (Case III) was felt clinically to possibly have a bone tumor. The presence of definite asymmetry in the two wrists and the apparent age of onset in the pre-adolescent period would favor Madelung's disease as classically described rather than dyschondrosteosis, which has been reported as a more symmetric process. However, the diagnosis of dyschondrosteosis is confirmed by the severe upper extremity mesomelia, even though asymmetric, with equal mesomelia of the lower extremities, short stature, a somewhat short lower segment and bilateral clinical and roentgenographic findings in the wrists. This patient's mother (Case IV) showed marked roentgenographic changes in both wrists along with short stature, short arm span, short lower segment, and lower extremity mesomelia, which confirmed the diagnosis. The atypical features in this case are lack of upper extremity mesomelia and the absence of clinical findings in the wrist. The changes in the humerus in this patient have been described in dyschondrosteosis and, when as marked as in this patient, result in a relatively normal ratio between the proximal and middle segments of the upper extremity. Case V, the third affected member of this family, a 15 year old boy, showed no clinical findings in the wrist and his height was within the normal limits for age although short in comparison to his brother and father. The diagnosis of dyschondrosteosis is substantiated by the typical though mild roentgenographic wrist findings, mild mesomelia, short lower segment, a somewhat short arm span, and the presence of other affected individuals in the family. It may be that this condition is less fully expressed in the male. Another factor which may explain the absence of previously reported male cases is the willingness of a man to accept a mild wrist deformity, which is not functionally disabling, while a woman is more likely to seek medical advice about a deformity of the same degree for cosmetic reasons.

In the third family, the 13 year old boy (Case VI) had a roentgenographic examination of the hands for a reason totally unrelated to the obvious clinical deformity. His mother had sought medical advice regarding her scoliosis but not for the functionally unimportant wrist deformity. Both were short, the boy particularly in relationship to his 2 normal younger siblings, but the normal father was a relatively small 164 cm. male and the affected boy's short stature was not considered unusual by the family.

Individuals with dyschondrosteosis have been reported in the English literature under the eponym, Madelung's disease, which in the past referred only to the obvious wrist deformity. It is generally conceded that the wrist deformity of dyschondrosteosis is identical clinically and roentgenologically to that of Madelung's disease. However, Madelung's disease has been differentiated from dyschondrosteosis in the European literature on the basis of the following points·

1. Madelung's disease is generally considered to have its onset in the pre-adolescent period.
2. It is usually thought to be associated with pain on motion of the joint.
3. Small stature and abnormalities of the lower extremities, humerus or radial head have not been mentioned.

4. The deformity is described as being unilateral in some instances.

However, the validity of these supposedly differentiating points is minimized, if not negated, by the study of the review of Anton, Reitz, and Spiegel[1] on Madelung's disease. Of their 171 cases, the great majority (127) showed bilateral changes. Only 42 had unilateral findings and 2 were not specified. Of 153 cases in which the age of onset was mentioned, 20 were noted by the age of 6 years. On the basis of the findings in the second family in this report, it seems probable that minor degrees of mesomelia are not observed by the parents and, without roentgenographic study, the wrist deformity is not appreciated until it is accentuated by early epiphyseal fusion in the pre-adolescent period. Indeed, as seen in Case IV, who had severe roentgenographic findings in the wrist as well as mesomelia of the lower extremities, clinical Madelung's deformity may never be apparent. Moreover, as illustrated in this same patient, if the humeri are also severely affected and therefore abnormally short, mesomelia of the upper extremity may be absent.

Of 137 cases, 37 were asymptomatic and in many others, the symptoms were trivial and of short duration. Examination of some of the original reports included in the review of Anton *et al.* suggests that in many instances, no symptoms were present at the time of study but were elicited by direct questioning. Stature was rarely mentioned but 10 patients were specifically noted to be short. Other bone abnormalities were occasionally reported and included cubitus valgus, tibial curvature, absence of the humeral head and deformity of the humeral tuberosity, short arms and legs, brachydactylia, and exostosis of the tibia and fibula. Many of these have been reported in dyschondrosteosis also.

In approximately 30 per cent of the cases where a hereditary pattern was noted, the mode of transmission was autosomal dominant, as is the case in dyschondrosteosis. A striking feature was the overwhelming predominance of females—a ratio of 4 to 1. Although a documented report of a male case of dyschondrosteosis has not been found, most authors have neither made roentgenograms nor measurements of male relatives of affected females. Several authors have mentioned that male relatives of their subjects had similar deformities. Patients V and VI represent the first descriptions of males who fit the criteria for dyschondrosteosis.

It is the author's opinion that the forearm deformity is primarily a result of unequal growth of the epiphyseal plate of the distal radius. For this reason, it may not become clinically noticeable until the early adolescent growth spurt occurs. Degrees of malformation in the other epiphyseal areas may give rise to the phenotypic spectrum evident in the cases presented. It would appear that the terms Madelung's disease and dyschondrosteosis have been used to describe the same condition. Indeed, with this idea in mind and when enough case data are reported, it is not difficult to find reports of Madelung's disease which violate the supposed differential points and fit neatly into the category of dyschondrosteosis.[1,7]

Madelung's deformity of the wrist is the most striking feature of dyschondrosteosis, and it is felt that all cases presenting this roentgenographic deformity bilaterally, except when it can be established to be secondary to trauma or infection, should be included under the heading of dyschondrosteosis. Dyschondrosteosis seems a preferable term to the eponym, "Madelung's disease," because it is more descriptive and because historically it has been applied to all dysplasias including the mesomelia, which is present in this condition.

SUMMARY

Seven cases of dyschondrosteosis are reported. This is a hereditary bone dysplasia with an autosomal dominant mode of transmission characterized by a typical de-

formity of the distal radius and ulna and proximal carpal bones and mesomelic dwarfism. The wrist deformity has been widely reported in the medical literature under the eponym, Madelung's disease.

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ROENTGENOLOGY OF THE CONGENITAL ADRENOGENITAL SYNDROME*

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HYPERADRENAL corticism may present in infancy and childhood as Cushing's syndrome, primary aldosteronism, feminizing adrenal neoplasm, and the adrenogenital syndrome. The latter results from adrenal hyperplasia or neoplasm and is the most common.[40] The congenital form of the adrenogenital syndrome results from adrenal hyperplasia and is the subject of this communication. Because the roentgenologist may be the first consultant to evaluate a patient with the congenital adrenogenital syndrome, he may be in a position to suggest the correct diagnosis. In addition, he can play an important role in judging the adequacy of treatment. For these reasons and because a comprehensive discussion of the roentgenology of the congenital adrenogenital syndrome has not appeared, this study was undertaken.

CLINICAL AND BIOCHEMICAL BACKGROUND

The congenital adrenogenital syndrome is a heritable inborn error of metabolism transmitted by an autosomal recessive gene which may be present in 1 per 125 individuals in the general population.[40] Virilization and rapid somatic growth occur in all patients who survive infancy and who do not receive proper medical therapy. In the female, evidence of virilization is present at birth but may not be noted in the male for 2 or 3 years. The congenital adrenogenital syndrome is the commonest cause of female pseudohermaphrodism. Virilization of a female beginning postnatally is rarely the result of adrenal hyperplasia and is usually due to an adrenal neoplasm.[3,29]

In the congenital adrenogenital syndrome, an enzymatic defect exists in the metabolic pathway, leading to cortisol production so that hydroxylation does not occur at certain key positions in the steroid molecule. As a result, there is an excessive accumulation of those intermediate steroids which are formed prior to the metabolic block and a deficient production of cortisol and other steroids which are normally the end products of the biosynthetic pathway.[2] Some of these intermediate steroids are converted into androgenically active substances. Since adrenal cortical activity begins in the fetus about the third month of gestation, the affected female is exposed to an excess of these androgenically active substances from her own abnormal adrenal cortex. The result of this androgenic environment is virilization of the female external genitalia. Although the internal female duct system and the gonads are not affected by this environment, the phallus is enlarged and there may be varying degrees of labioscrotal fusion.[2,8,16] In rare instances, the labioscrotal fusion may be so extensive that the urethra traverses the clitoris. Similar masculinization of the female external genitalia can also occur in the newborn female whose mother received androgens, synthetic progestins, or from a maternal androgen secreting neoplasm during the critical period of gestation (Table I).[6]

The defect in cortisol synthesis is accompanied by endogenous pituitary adrenocorticotrophic (ACTH) stimulation with subsequent enlargement of the target gland, the adrenal.[2] Since cortisol is necessary for regulation of the pituitary-adrenal axis, there is no inhibition of this trophic hormone. Intermediate steroid synthesis is accelerated and these substances are present in greatly increased amounts. Some of the urinary metabolites of these intermediate steroids which are useful in the diagnosis and management of patients with the con-

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TABLE I

DIFFERENTIAL DIAGNOSIS OF THE VIRILIZING CONGENITAL ADRENOGENITAL SYNDROME

Female		Male	
Clinical Manifestations	Differential Diagnosis	Clinical Manifestations	Differential Diagnosis
Neonatal female pseudohermaphrodism	1. True hermaphrodism with ovary and testis or ovarotestis 2. Nonadrenal female pseudohermaphrodism a. As a congenital anomaly associated with other anomalies b. Secondary to maternal androgens from masculinizing neoplasms, exogenous androgens or progestins administered to the mother during gestation 3. Male pseudohermaphrodism a. Spontaneous feminization of a male fetus b. Secondary to estrogens administered to the mother during gestation	Infantile or childhood macrogenitosomia praecox	1. Adrenal cortical neoplasms 2. Testicular neoplasms 3. Precocious puberty
Infantile or childhood virilism	1. Adrenal cortical neoplasms 2. Virilizing ovarian tumors a. Arrhenoblastoma b. Hilus cell tumors } very rare c. Adrenal cell tumors		

genital adrenogenital syndrome include the total 17 ketosteroids, pregnanediol, and pregnanetriol.[6] Treatment of the congenital adrenogenital syndrome with cortisol and related compounds in proper dosage for an indefinite period serves to supply the deficient hormone as well as to suppress ACTH secretion by the pituitary.

In the male with the congenital adrenogenital syndrome, sexual precocity is generally not recognized until 2 or 3 years after birth, and the differentiation between this and the acquired form of the syndrome may be difficult. The differential diagnosis can be made in both sexes by studying the effects of cortisol administration upon the urinary excretion of the total 17 ketosteroids and of pregnanetriol. After adequate replacement therapy with cortisol, the 17 ketosteroids and pregnanetriol values in the urine decrease to normal levels while in the presence of a hormone secreting neoplasm, there will usually be little or no change. In addition, pregnanetriol is much more likely to be found in the urine of a patient with the congenital adrenogenital syndrome while dehydroisoandrosterone is more likely to be found if there is a hormone secreting adrenal neoplasm.[18,26]

Most patients with the congenital adrenogenital syndrome do not have clinical evidence of adrenal insufficiency; that is to say, small but adequate amounts of cortisol are produced in the adrenal glands. In about 30 per cent of patients with the congenital adrenogenital syndrome, the biosynthetic block is more complete and there is failure of adequate cortisol formation.[2] This is the most commonly diagnosed type of adrenal crisis in the perinatal period.[30] Early diagnosis is imperative in this group who, if untreated, will almost certainly die during the first months of life. Vomiting is the cardinal symptom of the congenital adrenogenital syndrome with adrenal insufficiency and is present in more than 90 per cent of cases. Projectile vomiting occurs in about 22 per cent. At the time of hospitalization, more than 90 per cent of these infants show clinical evidence of dehydration and emaciation.[17] Not infrequently, these patients will be referred to the roentgenologist for gastrointestinal examination. Inspection of the external genitalia in infants before proceeding with the fluoroscopic evaluation of the intestinal tract is, therefore, just as important as taking a history in adult patients. Hypertrophy of the clitoris and ventral bending as in chordee with variable fusion of the labioscrotal folds are present in more than 95 per cent of female patients (Fig. 1, *A* and *B*). It must be recalled that many of these females will be referred as males with male names. In no case of Iversen's series of 135 patients with failure of adequate cortisol production was hypertrophic pyloric stenosis found at postmortem examination or at the time of exploratory surgery.[17]

Because of the deficiency of the adrenal cortical hormones influencing electrolyte metabolism, there result a marked reduction of the serum sodium concentration and elevation of the serum potassium. These electrolyte aberrations result in disturbance of cardiac rate and rhythm.[20] Vomiting will further exaggerate these electrolyte disturbances as well as increase the severity of the dehydration. A patient may thus be suspected of having congenital heart disease with the presenting findings of cyanosis, circulatory collapse and cardiac arrhythmia.

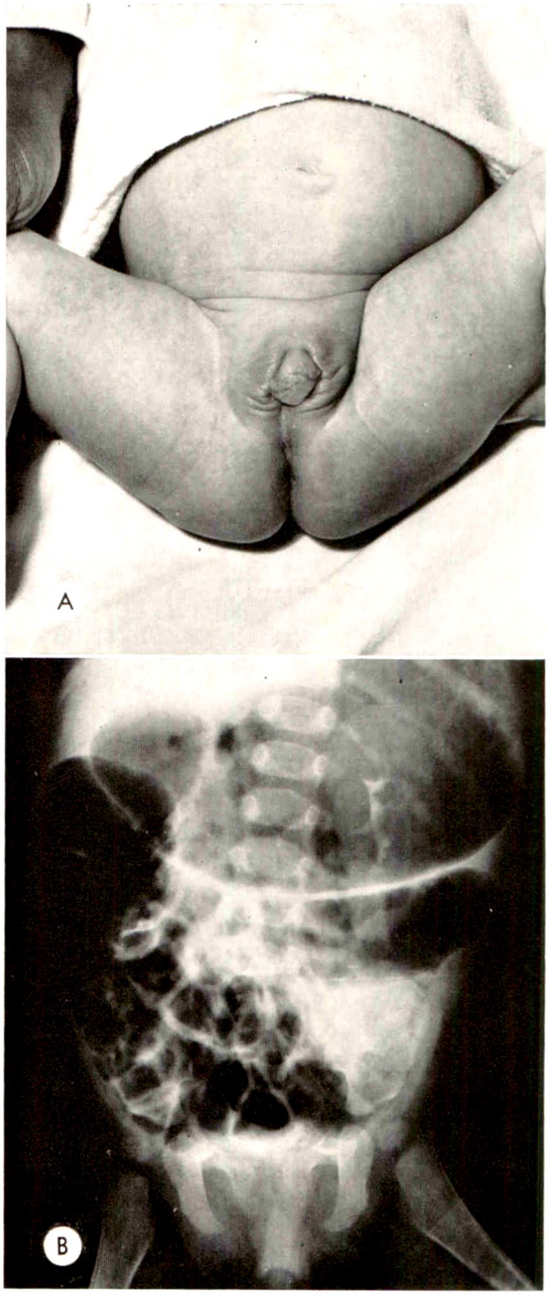


Fig. 1. (*A*) External genitalia of a 6 day old female with the congenital adrenogenital syndrome. Clitoral hypertrophy and ventral bending are evident. (*B*) Excretory urogram of the same patient several months later demonstrates the large phallus in a female infant.

Only about one-third of patients have the most severe or "salt-losing" form of the congenital adrenogenital syndrome described above. The majority have simple virilism without other symptoms.[39] In the male, despite penile enlargement, the testes remain small. This feature is of value in differentiating the congenital adrenogenital syndrome from patients with constitutional sexual precocity or hypothalamic-pituitary disturbances. In the female, the genital malformations generally take one of five different forms (Fig. 2).[26] Common to all

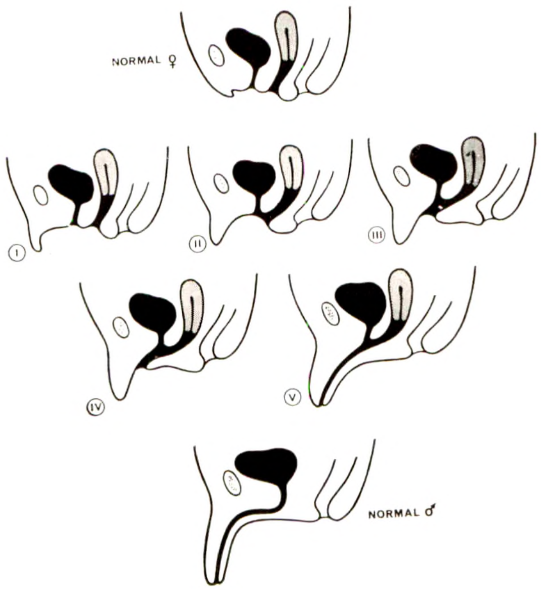


Fig. 2. Five forms of genital malformations encountered in the female with the congenital adrenogenital syndrome. (After Prader *et al.*[27])

five forms is hypertrophy of the clitoris. In Type I the vulva is normal. In Type II the vestibule is deep and funnel shaped. Types III and IV are associated with a single perineal urogenital orifice of variable size. In Type V the urogenital orifice is at the tip of the clitoris. The labia minora are absent in Types III, IV and V and the labioscrotal folds are increasingly fused. The vagina opens directly to the outside in Types I and II and into the urogenital sinus in Types III, IV and V. Types I and V are very rare. When virilism is associated with the salt-losing form, Type IV is usually present. Aside from these abnormalities, the sexual differentiation is entirely female. A uterus, oviducts and ovaries are present. It should be emphasized that on rare occasions genital abnormalities similar to those seen in the congenital adrenogenital syndrome may occur without adrenal disease in otherwise normal patients.[28]

Untreated patients of both sexes with simple virilism grow rapidly during the first years of life and acquire sexual hair, acne, and a deep voice. There is rapid somatic maturation with advance in epiphyseal ossification.[2] During the first several months or year of life, however, epiphyseal maturation is generally normal with rapid progression thereafter.[1] Associated with this is rapid muscular development resulting in the classic "infant Hercules." In 8 or 10 years, growth may be complete, and the child resembles an adult with short legs and broad shoulders. Thus, there is a dissociation between the normal parallel relationship between growth and maturation. Premature epiphyseal fusion produces the paradox of a dwarfed adult in a child who was unusually tall for his chronologic age.[40]

About 13 years ago, the congenital adrenogenital syndrome with virilism and systemic hypertension was described. Since that time cases have been recorded in children with cardiovascular accidents, myocardial infarction, and congestive heart failure resulting from hypertension.[5] In a large series of patients with the congenital adrenogenital syndrome about 5 per cent will have virilism associated with hypertension.[39] Other exceedingly rare types of the congenital adrenogenital syndrome are virilism and polycythemia, virilism and pyrexia, virilism and hypoglycemia, and feminization of the male infant.[6]

Affected siblings and closely related relatives manifest the same clinical form of the disease, suggesting a genetic independence of the 3 basic clinical types: (1) simple virilism, (2) virilism and adrenal insufficiency and (3) virilism with hypertension.[27]

ROENTGENOGRAPHIC MANIFESTATIONS

With a background in the biochemical and resultant clinical features of this illness, the roentgen manifestations become more clear. Roentgenograms and case records of 43 patients with the congenital adrenogenital syndrome have been reviewed as a basis for this study. Some patients were referred after the diagnosis had been established but the majority were referred to the Indiana University Medical Center as undiagnosed cases. Six patients in this series are described briefly to emphasize the various roentgen features.

CONGENITAL ADRENOGENITAL SYNDROME WITH ADRENAL INSUFFICIENCY IN A MALE

One-third of the patients with the congenital adrenogenital syndrome present with virilism and adrenal insufficiency. A history of vomiting, dehydration, diarrhea, circulatory collapse or cyanosis may be obtained. Dehydration may be manifested on the frontal chest roentgenogram by reduction in soft tissue thickness best appraised along the lateral chest wall at the thinnest portion. At a 72 inch focus film distance a thickness of less than 4.5 mm. is suggestive of dehydration in an infant beyond 1 week of age.[23] The lungs may be overinflated from the increased rate and depth of respiration. The heart is generally normal in size or sometimes small. This occurs because of the low position of the diaphragm in the hyperinflated chest as well as from the reduced intravascular volume.[19,36]

Case i. F.W. was a male seen at 2 weeks of age because of failure to gain weight and cyanosis which was noted 2 days prior to admission. The diagnosis of the congenital adrenogenital syndrome with adrenal insufficiency was established. A frontal chest roentgenogram at the time of admission (Fig. 3) showed thin soft tissues along the lateral chest wall which measured 3 mm. at the thinnest point. The hyperlucent lungs resulted from slight overinflation and the paucity of soft tissue over the chest wall.

CONGENITAL ADRENOGENITAL SYNDROME WITH VIRILISM AND ADRENAL INSUFFICIENCY

Vomiting may prompt examination by plain supine roentgenograms of the abdomen. A pattern simulating high gastrointestinal obstruction with a paucity or absence of intestinal gas may be encountered, resulting perhaps from persistent vomiting acting like constant gastric suction.[33,37] Opaque contrast medium studies of the intestinal tract in the vast majority of cases will not outline an organic obstruction. Occasionally, gastric irritability may be encountered with spasm of the pylorus.[37] This should not be confused with the persistent characteristic roentgen findings in hypertrophic pyloric stenosis. It should be emphasized that when evaluating the upper intestinal tract of a young infant with dehydration, it is probably hazardous to use water soluble iodinated organic contrast media because of the hypertonicity of these substances.[15] They exert an osmotic gradient that tends to "pull" fluid from the vascular compartment and further dehydrate a patient already seriously or critically ill with dehydration.

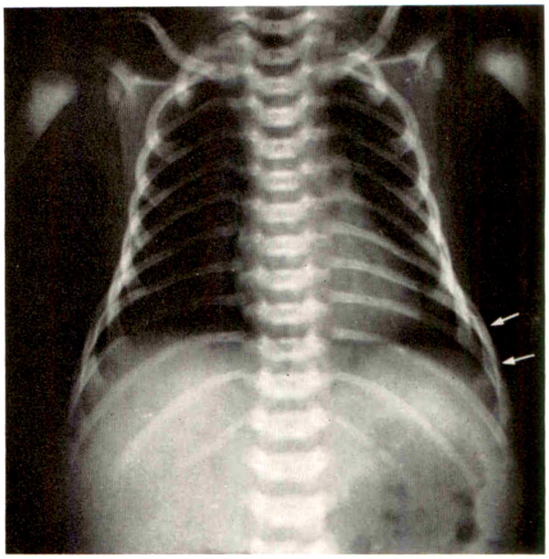


Fig. 3. Case i (F.W.). Frontal chest roentgenogram of a 2 week old infant with dehydration. The soft tissues along the lateral chest wall measure 3 mm. (arrows). The hyperlucent lungs result from slight overinflation and the paucity of soft tissue over the chest wall.

Case ii. K.S. was first seen at 6 weeks of age because of vomiting and dehydration. Physical examination indicated the presence of gastric waves but a pyloric tumor was not palpated. Roentgenograms of the stomach and duodenum were not typical of hypertrophic pyloric stenosis, but some delay in gastric emptying was noted (Fig. 4*A*). Abdominal exploration failed to reveal any gastrointestinal abnormalities. Subsequently, the diagnosis of the congenital adrenogenital syndrome with adrenal insufficiency was established. The patient was assumed to be a male and was so reared until the age of 5 years when examination of the scrotum failed to reveal the presence of gonads (Fig. 4*B*). The bone maturation age at this time was 13 to 14 years. It was learned

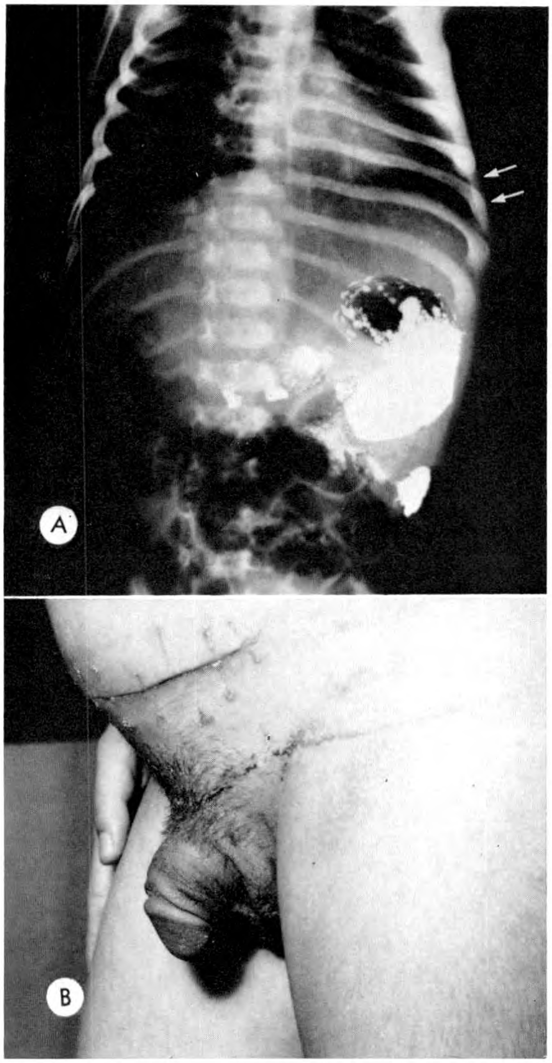


Fig. 4. (*A*) Case II (K.S.). Upper gastrointestinal study in a 6 week old infant with vomiting showing some delay in gastric emptying. The characteristic roentgen features of hypertrophic pyloric stenosis are not present. Note thin soft tissues over the chest wall (arrows). (*B*) Type V genital malformation as seen at the age of 5 years after exploratory laparotomy showed the presence of female internal genitalia.

that the steroid medication was taken irregularly. A buccal smear was suggestive of the female chromatin pattern and, subsequently, exploratory laparotomy established the presence of a uterus, oviducts, and ovaries. The external genital pattern corresponded to the rare Type V (Fig. 2).

CONGENITAL ADRENOGENITAL SYNDROME WITH SIMPLE VIRILISM

Advanced skeletal maturation is a feature common to all forms of the congenital adrenogenital syndrome after the first several months of life. Roentgen study of the hand and wrist is an excellent guide to the maturation of the patient as a whole.[13] Significant diversity may occur between development in the hand and wrist and other epiphyses in about 10 per cent of patients so that additional centers may be required for accurate appraisal of maturation.[22] In addition, there may be advanced pneumatization of the mastoids and paranasal sinuses as well as premature calcification of the cartilages of the ribs and larynx.[4,10]

Norms for the roentgenographic evaluation of tooth formation and root resorption have been provided in recent years.[9,11] This has proved to be of value in differentiating idiopathic sexual precocity from the congenital adrenogenital syndrome.[35] In the latter condition, tooth development is advanced for the chronologic age in contrast to idiopathic sexual precocity where there seems to be a dissociation between sexual development and skeletal maturation on the one hand and dental development on the other.

The precocious muscular development in these young children is striking. Roentgenograms of the extremities demonstrate large muscle masses for the chronologic age. Osseous prominences and skull diploë develop prematurely, secondarily to the advanced muscular development.[7,31]

Case III. P.C. was an 8 year old male who developed rapidly in height and body build. He had a large penis with pubic hair. The blood pressure was normal. Skeletal maturation as judged by the atlas of wrist and hand development was 14 years.[13] The diagnosis of the congenital adrenogenital syndrome was subsequently established. Roentgen examination of the arms (Fig. 5*A*) showed a striking degree of muscular development for a child with a chronologic age of 8 years. The diploic layer of the skull was also quite thick (Fig. 5*B*).

CONGENITAL ADRENOGENITAL SYNDROME WITH SIMPLE VIRILISM

The maturation age as determined by roentgenograms of the hand and wrist serves as a useful guide in following the adequacy of exogenous cortisol therapy. If the maturation age is maintained at a normal rate, the longitudinal growth tends to be slightly below average and, if growth is maintained at a normal rate, the maturation age advances slightly more rapidly than normal.[31] When excessive cortisol therapy is given, there is usually retardation of growth and maturation. A few cases of iatrogenic Cushing's syndrome have been reported as a result of excessive cortisol.[12] If the maturation age is in excess of 11 to 13 years at the time of initiation of cortisol treatment, true precocious puberty may develop. The explanation for this lies in the fact that cortisol inhibits ACTH from the pituitary and, secondarily, the excessive adrenal androgen production. Large amounts of these androgenic steroids inhibit pituitary gonadotrophins. Exogenous cortisol will thus permit secretion of the pituitary gonadotrophins and the development of puberty in accordance with the attained maturation age regardless of the chronologic age.[22]

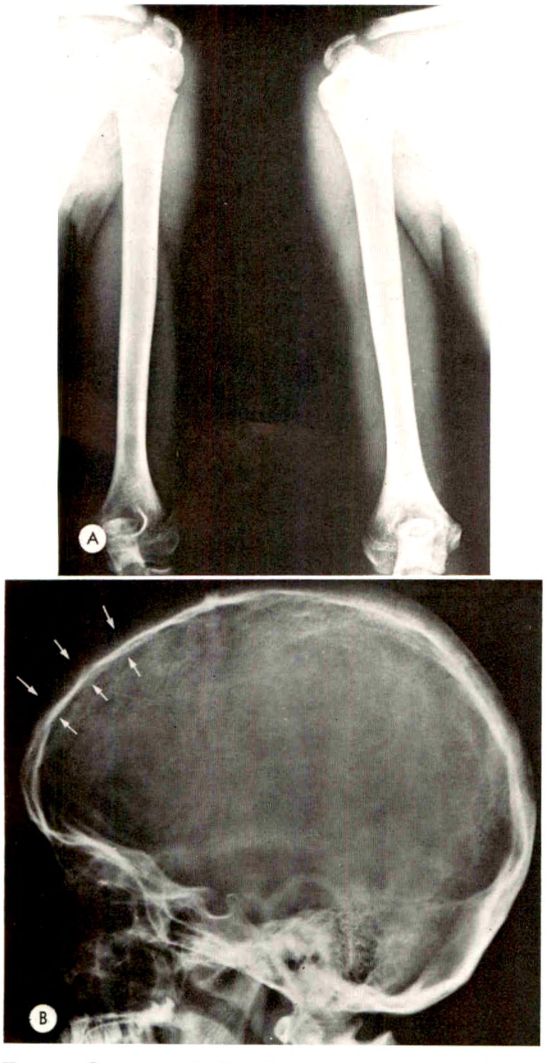


Fig. 5. Case iii (P.C.). Unusually well developed musculature of the arms in an 8 year old male with the congenital adrenogenital syndrome. Note advance in epiphyseal development. (*B*) Thick skull diploë is evident (arrows).

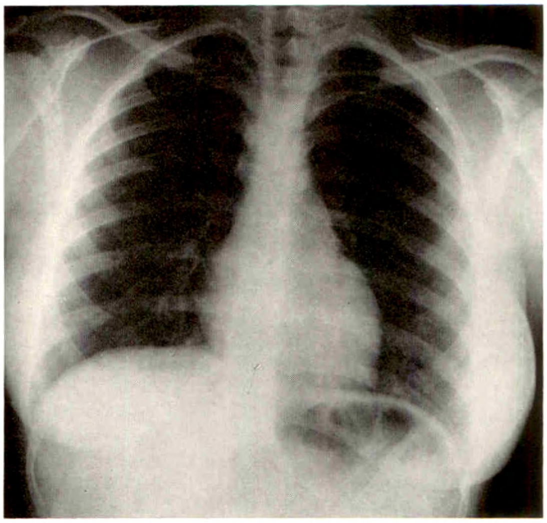
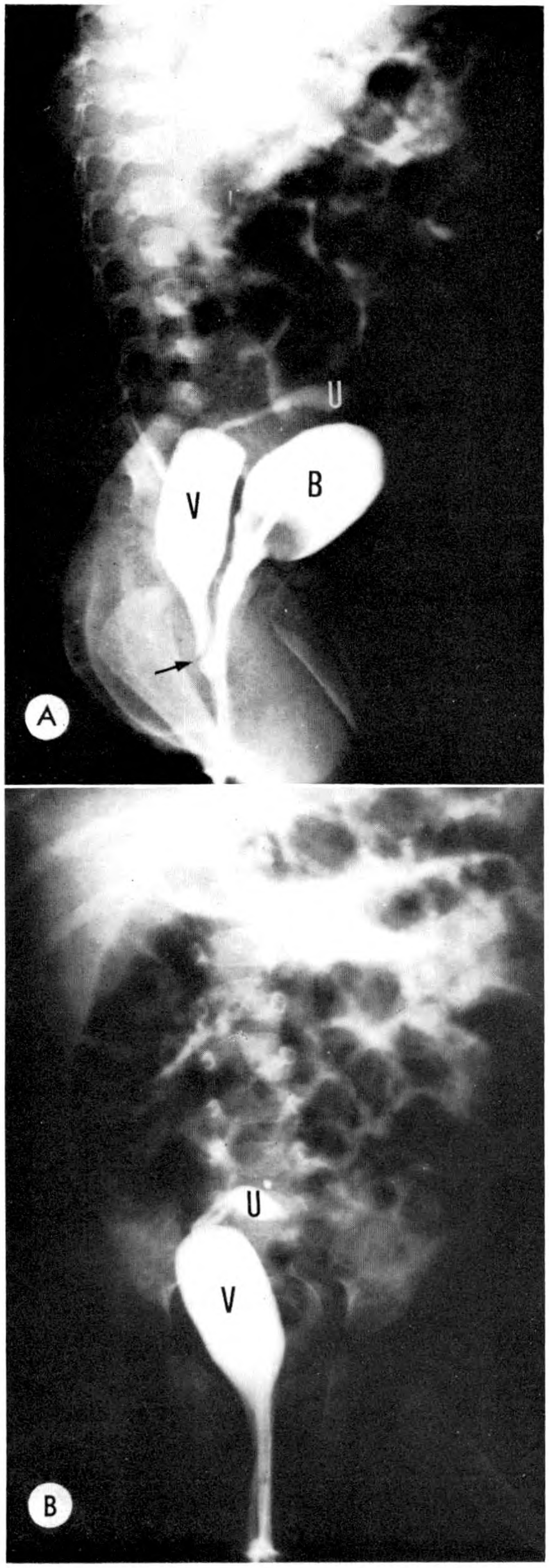


Fig. 6. Case iv (D.C.). Eleven year old female with marked breast development since the onset of cortisol therapy.

Case iv. D.C. was an 11 year old female known to have had a large clitoris since birth. When she was first seen at the age of 4 years, her skeletal maturation as determined by roentgen study of the hand and wrist was 12 years. Subsequent studies confirmed the diagnosis of congenital adrenogenital syndrome with simple virilism. After therapy with cortisone, breast development was noted. The frontal chest roentgenogram (Fig. 6) demon-



strates the marked degree of breast development at the age of 11 years in a child who was virilized.

CONGENITAL ADRENOGENITAL SYNDROME WITH VIRILISM AND ADRENAL INSUFFICIENCY

Roentgen evaluation of the genital tract in the congenital adrenogenital syndrome is helpful in defining the anatomy for possible surgical treatment.[14,24,34] With a firm rubber end hole catheter placed inside the urogenital sinus, water soluble iodinated organic contrast media may be injected into the vagina, bladder, and urogenital sinus. If this technique is not successful, a soft rubber catheter may be used to probe the urethral and vaginal orifices. Very often an indentation is detectable at the apex of the saccular vagina which results from the cervix. If the bladder cannot be identified by these methods, opacification may be obtained by excretory urography. When the urogenital sinus, urinary bladder, and vagina are outlined in a patient with a large phallus, one has not established the diagnosis of the congenital adrenogenital syndrome, since this same anatomic arrangement may be seen in male pseudohermaphrodism, female pseudohermaphrodism without adrenal hyperplasia and true hermaphrodism.[24]

Case v. L.W. was a female infant, first seen at 6 days of age because of vomiting and dehydration. She was noted to have a "small penis or large clitoris." The diagnosis of the congenital adrenogenital syndrome with adrenal insufficiency was established and appropriate therapy was instituted. At 5 weeks of age, a roentgen examination was performed to

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Fig. 7. Case v (L.W.). (*A* and *B*) Five week old female with the congenital adrenal genital syndrome and adrenal insufficiency. The genital malformation is Type iv. There is opacification of the bladder (B), vagina (V), and uterine cavity (U). The hymen is evident (arrow). A balloon catheter is present in the bladder, having traversed the urogenital sinus and urethra.

define the anatomy of the internal genitalia (Fig. 7, *A* and *B*). The bladder, vagina, uterine cavity, and oviducts opacified. The genital pattern conformed to Type IV (Fig. 2).

CONGENITAL ADRENOGENITAL SYNDROME WITH ADRENAL INSUFFICIENCY AND SUBSEQUENT HYPERTENSION (?)

About 5 per cent of patients with the congenital adrenogenital syndrome will have the enzymatic deficiency resulting in virilism and hypertension. This may be reflected on the chest roentgenogram by cardiac enlargement and, possibly, congestive heart failure.

Case VI. S.N. was an 8 day old female presenting with projectile vomiting. A large clitoris with a single opening at its base was noted. The labial folds had scrotal corrugations. Serum electrolyte concentrations and urinary steroid studies established the diagnosis of the congenital adrenogenital syndrome with adrenal insufficiency. A buccal smear suggested the female chromatin pattern. The patient was placed on appropriate therapy and discharged. Nineteen months later she was re-admitted for clitorectomy. A blood pressure recording in the arm was obtained for the first time during this admission. The systolic pressure was 180 mm. Hg and the diastolic pressure 130 mm. Hg. A frontal chest roentgenogram (Fig. 8) showed left ventricular enlargement. Extensive study failed to disclose a cause for this hypertension. Antihypertensive drug therapy was initiated with resultant reduction of blood pressure to normal levels. The combination of the congenital adrenogenital syndrome with adrenal insufficiency and hypertension appears to be unique in this patient. Continued follow-up and re-evaluation will be necessary to exclude the chance occurrence of hypertension of non-adrenal origin in a patient with the congenital adrenogenital syndrome and adrenal insufficiency.

Plain roentgenograms of the abdomen and excretory urography are of little or no value in the diagnosis of adrenal enlargement from adrenal hyperplasia in infancy. Extraperitoneal pneumography with laminagraphy could be used to outline the adrenal glands, but this is rarely necessary since the clinical and biochemical findings are generally diagnostic.[21,25,32]

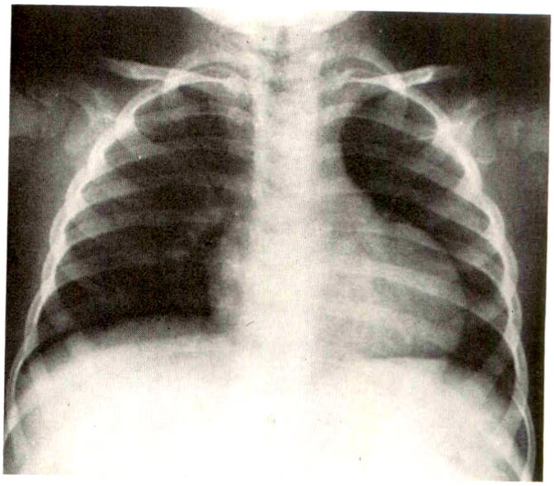

Fig. 8. Case VI (S.N.). Nineteen month old female with the congenital adrenogenital syndrome and adrenal insufficiency. A blood pressure of 180/130 was recorded. The concentric enlargement of the cardiac apex indicates left ventricular enlargement.

Four patients in this series developed septic arthritis of the hip joint at some time after the institution of cortisone therapy. Pneumonia was also a frequent occurrence which was documented on roentgenograms in more than 25 per cent of the patients at some time during the follow-up period. These infections must be recognized early in patients with the congenital adrenogenital syndrome whose adrenals have been suppressed by exogenous steroids, since the added stress may precipitate adrenal crisis unless supplemental steroid therapy is administered.[38]

SUMMARY

The congenital adrenogenital syndrome is a hereditary form of hyperadrenal corticism present at birth. The basic abnormality is an enzymatic defect in cortisol synthesis, resulting in adrenal hyperplasia and excessive adrenal androgen production. The three basic clinical types are: (1) simple virilism, (2) virilism and adrenal insufficiency, and (3) virilism and hypertension.

Although there are no pathognomonic roentgen findings several features are present which characterize patients with this disease. Six of a series of 43 cases are briefly reported to show some of these roentgen features.

Approximately 60 per cent of patients are of the type with simple virilism. Accelerated maturation is reflected roentgenographically in the skeleton, teeth, and muscular tissue. Five patterns of genital malformations in the female are listed, some of which can be best defined by roentgen analysis.

One-third of the cases have virilism and adrenal insufficiency. These patients present in early infancy with roentgen signs of dehydration such as pulmonary overinflation, reduced soft tissue thickness over the chest wall and sometimes a small transcardiac diameter. Plain abdominal roentgenograms may demonstrate a paucity or, occasionally, absence of intestinal gas.

The type associated with virilism and hypertension represents about 5 per cent of cases of the congenital adrenogenital syndrome. Cardiac enlargement and signs of passive pulmonary congestion may be evident on the chest roentgenogram.

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INTERVERTEBRAL DISK CALCIFICATION IN CHILDREN*

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INTERVERTEBRAL disk calcification in childhood is a relatively rare finding but has been reported with increasing frequency since 1945.[1,2,4] Two additional cases of this interesting entity are presented here, 1 case of symptomatic calcification of the 3rd thoracic intervertebral disk and the second of asymptomatic calcification of the cervical disk between the 4th and 5th cervical vertebrae.

REPORT OF CASES

CASE I. A 6 year old Caucasian female was admitted to Los Angeles County General Hospital with chief complaints of irritability and intermittent left anterior chest pain radiating to the interscapular region. The pain had become more severe in the 48 hours prior to admission. The night prior to admission, she was noted to have neck stiffness. The patient had had an upper respiratory infection 2 weeks prior to admission with no apparent sequelae until the onset of above symptoms.

Vital signs on admission were normal, and the patient was afebrile. The pertinent physical findings were nuchal rigidity, allowing only about a 20° flexion from the vertical, slight right thoracic scoliosis and right thoracic paravertebral muscle spasm with splinting. The patient's neurologic examination was normal.

Routine blood cell count and urinalysis on admission were normal. A 24 hour urine specimen for homogentisic acid was negative.

Lumbar puncture showed clear spinal fluid. There was only one cell present, and no segmented neutrophils were noted. Cerebral spinal fluid sugar was 66 mg./100 ml., chloride 119 mEq./l., protein 22 mg./100 ml. Culture of the spinal fluid revealed no growth. Skin tests for coccidioidomycosis, histoplasmosis and tuberculosis were negative. Gastric washings were negative for acid fast bacilli.

Roentgenograms (Fig. 1, *A* and *B*) of the entire spine revealed calcifications of the annulus fibrosus anteriorly and the nucleus pulposus posteriorly in the 3rd thoracic disk. Laminagrams (Fig. 1*C*) clearly confirmed the calcification of the nucleus pulposus.

The patient's symptoms, except for mild pain in the thoracic area on flexion, cleared 2 days after admission, and she was discharged considerably improved after 4 days. However, according to the mother, she continued to have mild discomfort at home for an additional 2 weeks. Follow-up roentgenograms 5 months after discharge revealed approximately 75 per cent regression of the intervertebral disk calcification. The patient has remained asymptomatic for 1 year.

CASE II. A 5 year old Negro male was seen in the Outpatient Department of the Los Angeles County General Hospital because of head trauma sustained in a fall. There was a brief period of unconsciousness. The only complaint on entry was neck pain.

On physical examination, the patient demonstrated torticollis with the head deviated and rotated slightly to the right. There was marked spasm of the right posterior cervical muscles but no point of tenderness.

Roentgenograms of the skull and spine revealed no fractures. There were both central and peripheral calcifications of the intervertebral disk between the 4th and 5th cervical vertebrae (Fig. 2). A review of a chest roentgenogram made 2 months previously showed that the disk was not calcified at that time. Disk calcification in this case is felt to be an incidental finding.

The patient was given symptomatic treatment and failed to return.

DISCUSSION

Intervertebral disk calcification has been known for a long time,[1] being first described by Luschka in 1858.[3] The calcifications

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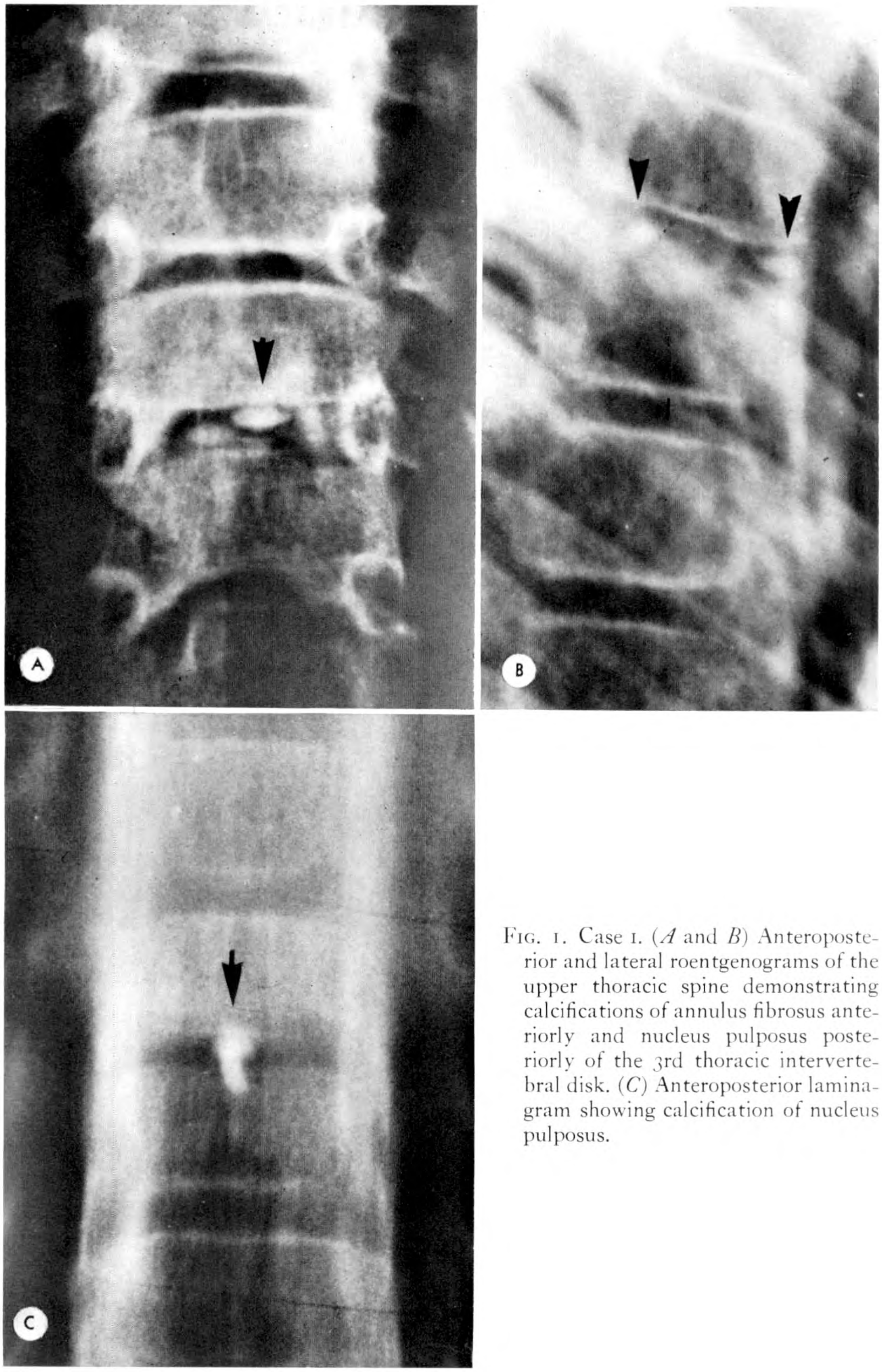

Fig. 1. Case 1. (*A* and *B*) Anteroposterior and lateral roentgenograms of the upper thoracic spine demonstrating calcifications of annulus fibrosus anteriorly and nucleus pulposus posteriorly of the 3rd thoracic intervertebral disk. (*C*) Anteroposterior laminagram showing calcification of nucleus pulposus.

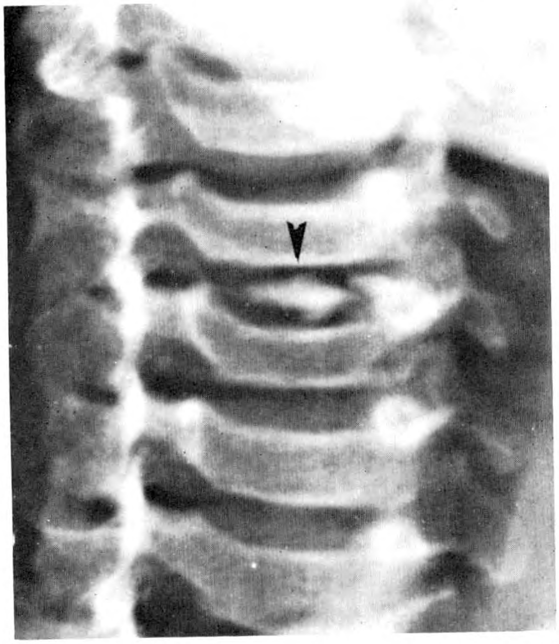

FIG. 2. Case II. Roentgenogram showing central and peripheral calcification of 4th cervical disk.

were first demonstrated roentgenographically by Beneke in 1897.[2] Later, Baron in 1942, described intervertebral disk calcification in the pediatric age group and Weens[5] was the first to describe it in children in this country.

In an excellent summary in 1963, Melnick and Silverman[2,4] reported 5 cases of their own, making the total number of reported cases 53. The etiology remains unknown. The character of this calcification is variable. It may be round, oval, fragmented, central, and/or peripheral.

When clinical symptoms are reported, they usually involve the cervical area; however, calcifications seen in the lumbar area usually are incidental findings. The calcifications in the thoracic spine caused pain, spasm, torticollis, and tenderness in one of our patients to such a degree that meningitis was seriously considered.

The role of trauma is difficult to evaluate and probably not related to intervertebral disk calcification. Fortunately, in Case II, a roentgenogram 2 months before injury was normal, calcification having occurred during the interim, prior to the injury. The onset and duration of disk calcification are difficult to estimate because the actual time of appearance is seldom known and, in many instances, serial follow-up observations are not made.

CONCLUSIONS

A case of symptomatic intervertebral disk calcification in a 6 year old Caucasian female involving the 3rd thoracic intervertebral disk and a case of asymptomatic intervertebral disk calcification in a 5 year old Negro male involving the 4th cervical disk are reported.

It is emphasized that intervertebral disk calcification in childhood is a benign condition and symptomatic therapy is all that is indicated.

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TRAUMATIC PNEUMOPERITONEUM IN THE NEWBORN*

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PNEUMOPERITONEUM in the newborn infant is usually the result of gastrointestinal perforation, which most frequently is secondary to intestinal obstruction.[26,28] Traumatic intestinal perforation with pneumoperitoneum in this age group has been reported only rarely. Three case reports of gastric perforation following tube feeding or intubation and resuscitation have been published.[8,15,19] Ten cases have been reported of rectal or rectosigmoid perforation resulting from barium, hypaque or cleansing enemas.[12,23,29,32] Perforation of the rectum by a thermometer in the newborn infant has been infrequently reported, and only 4 cases with pneumoperitoneum have appeared in the English language literature.[6,10,15,25]

The purpose of this paper is twofold: (1) to report an additional case of perforation of the rectum by a thermometer in a premature infant with pneumoperitoneum, and (2) to describe our experience with 17 other cases of pneumoperitoneum and 10 cases of intestinal perforation without pneumoperitoneum in the first few weeks of life.

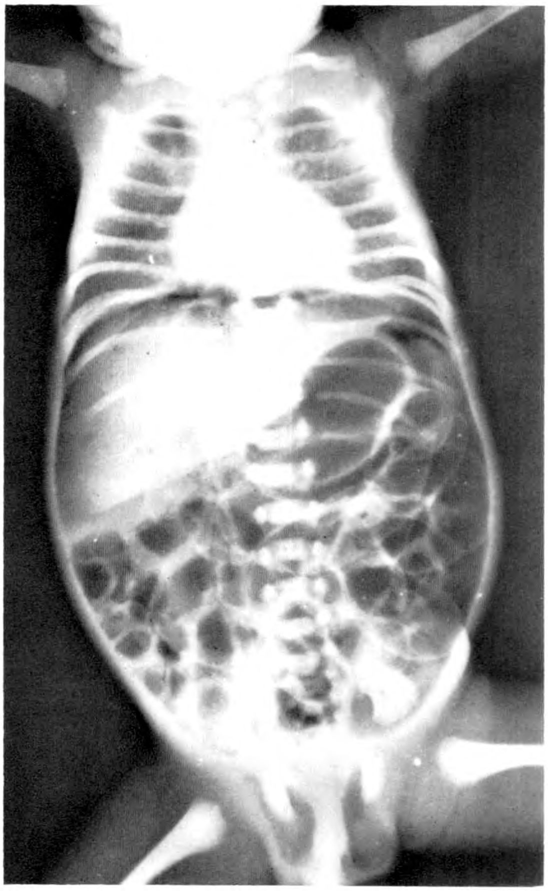

FIG. 1. Note the free air in the scrotum, under the diaphragm, and outlining the lateral peritoneal walls and falciform ligament. Both inner and outer walls of bowel loops are visualized.

REPORT OF A CASE

A three day old Caucasian male was transferred to Los Angles County General Hospital on June 17, 1964, following spontaneous vaginal delivery at 30 weeks of gestation. The birth weight was 3 pounds, 5½ ounces. Slight cyanosis was noted at birth, but the baby's condition was stable until the third day of life. At this time, moderate cyanosis, respiratory distress, and abdominal distention developed. The body temperature was 95° F. rectally. Small amounts of meconium were passed. A roentgenogram of the abdomen on admission (Fig. 1) revealed extensive pneumoperitoneum. At surgery, a perforation of the anterior wall of the rectum was found, just above the peritoneal reflection, approximating the diameter of a thermometer bulb. Meconium was leaking from the perforation, and there was early abscess formation. The perforation was closed, but the patient expired during the colostomy procedure. At autopsy, there was no evidence of malrotation or bowel obstruction. Gross and microscopic examination revealed no abnormalities in the vasculature, ganglion cells, or smooth muscle. The bowel wall was intact except for

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TABLE I

INFANTS WITH INTESTINAL PERFORATION AND EVIDENCE OF PNEUMOPERITONEUM

Case No.	Age at Diagnosis of Pneumoperitoneum	Race and Sex	Maturity	Diagnosis	Outcome
1	3 da.	C/M	P	Perforation of rectum by thermometer; peritonitis	Expired
2	3 da.	C/M	P	Spontaneous perforation of distal ileum; peritonitis	Expired
3	7 da.	N/M	T	Spontaneous perforation of greater curvature of stomach; peritonitis	Expired
4	4 da.	N/M	T	Hemorrhagic pneumonitis—no perforation found; no peritonitis	Expired
5	2 da.	N/M	P	Perforation of the cecum due to necrotizing colitis; peritonitis	Expired
6	3 wk.	N/F	P	Spontaneous perforation of transverse colon; incomplete malrotation without volvulus; stippled epiphyses; pulmonary stenosis and ventricular septal defect; peritonitis	Expired
7	7 da.	C/F	T	Operation for jejunal atresia; postoperative perforation of distal ileum; peritonitis	Expired
8	5 da.	N/F	T	Spontaneous perforation of greater curvature of stomach; peritonitis	Recovered
9	2 da.	C/M	T	Unknown—no surgery	Recovered
10	8 wk.	C/M		Perforated ulcer in greater curvature of stomach; peritonitis	Expired
11	3 mo.	N/F	T	Postoperative atresia of common bile duct; perforated terminal ileum proximal to obstruction by postoperative band; situs inversus of liver and stomach; peritonitis; biliary cirrhosis	Expired
12	3 da.	N/M	T	Spontaneous perforation of lesser curvature of stomach; peritonitis	Expired
13	2 wk.	N/M	T	Volvulus of small bowel with perforation of ileum; peritonitis	Expired
14	1 da.	C/M	P	Volvulus of terminal ileum with perforation; no malrotation; peritonitis	Expired
15	2 wk.	C/M	T	Gas peritonitis and enteritis; no perforation; coarctation of aorta	Expired
16	3 mo.	C/M	T	Postoperative Hirschsprung's disease with colostomy; ileal perforation due to accidental laceration at surgery; peritonitis	Expired
17	5 da.	C/F	P	Perforated gastric ulcer of posterior wall; peritonitis	Expired
18	5 wk.	N/M	T	Incarcerated inguinal hernia with gangrenous perforation of terminal ileum; peritonitis	Expired

C= Caucasian. N=Negro. P=Premature. T=Term.

the surgically closed perforation. Death was ascribed to accidental rectal perforation with peritonitis.

DISCUSSION

There is little reason to doubt that the perforation of the rectum was caused by the insertion of a thermometer. In the infant, the anorectal anatomy predisposes to perforation by an instrument, because of the anterior angulation at the anorectal junction. An object inserted into the axis of the anal canal will strike the anterior rectal wall unless re-directed posteriorly. In the cases of perforation by thermometer

Table II

INFANTS WITH INTESTINAL PERFORATION WITHOUT ROENTGENOGRAPHIC EVIDENCE OF PNEUMOPERITONEUM

Case No.	Age at Diagnosis	Race and Sex	Maturity	Diagnosis	Outcome
1	1 mo.	C/F	P	Omphalocele (repaired); perforated duodenal ulcer; bronchopneumonia; peritonitis	Expired
2	2 da.	C/F	T	Mongol; esophageal atresia; perforated duodenal ulcer; peritonitis; aspiration pneumonia; patent ductus ateriosus; ventricular septal defect	Expired
3	5 da.	C/F	T	Perforated duodenal ulcer; peritonitis; pneumonia; septicemia	Expired
4	2 mo.	N/F	T	Perforated duodenal ulcer; peritonitis; septicemia	Expired
5	3 mo.	C/F	T	Systemic moniliasis; perforated duodenal ulcer; peritonitis	Expired
6	6 mo.	C/M	T	Meckel's diverticulitis with perforation of adjacent ileum	Recovered
7	12 da.	C/F	P	Hirschsprung's disease with perforation of transverse colon; patent ductus arteriosus	Expired
8	4 da.	N/M	T	Duodenal atresia; acute jejunal ulcers with perforation; peritonitis	Expired
9	2 mo.	C/M	P	Congenital band obstruction and perforation of distal ileum	Recovered
10	4 mo.	C/M	T	Perforated duodenal ulcer; peritonitis; transposition of great vessels; atrial septal defect; ventricular septal defect; intracranial sinus thrombosis	Expired

C=Caucasian. N=Negro. P=Premature. T=Term.

previously cited, and in a case without pneumoperitoneum reported by Warwick and Gikas,[31] the perforations were found in the anterior wall of the rectum. The majority of the enema-induced perforations mentioned earlier were also in the anterior wall of the rectum or rectosigmoid.

While there are reports of spontaneous rectal and rectosigmoid perforations in the normal colon in adults,[3,7,13,14] there is no such reported case in an infant.[19] Ross reported the case of a 1 year old child in whom the thermometer was actually found in the peritoneal cavity.[22] Such incontrovertible evidence of perforation by thermometer is infrequent. It would seem reasonable, therefore, to conclude that death in the case herein reported was due to accidental perforation of the rectum by a thermometer.

The roentgen signs of pneumoperitoneum have been well described,[16,21,24] and the diagnosis of pneumoperitoneum is, in general, not difficult. However, the etiology of the pneumoperitoneum is frequently not ascertained preoperatively. In some cases, the site of perforation may not be found, either at surgery, or at autopsy.[4,5,20]

The experience at the Los Angeles County General Hospital over the past 15 years with cases of pneumoperitoneum in the neonatal and infant period is summarized in Table I. Sixteen of the 18 infants died. This mortality rate of 89 per cent is not unusual. Nice and Mouton[17] reported a 75 per cent mortality in their series of 16 cases. Freeark *et al.*[10] had an 87 per cent mortality in 15 cases, and Tucker and Izant[29] a 50 per cent mortality in 26 cases.

Table II summarizes the cases of intestinal perforation in the same age group for a similar period of time, in which pneumoperitoneum was not demonstrated. Mortality in this group was 80 per cent. It is of interest that only about 60 per cent of intestinal perforations in our series had roentgenographic evidence of pneumoperitoneum.

There are many causes of pneumoperitoneum in infants. Some are understood; others are obscure. Examples of the latter are necrotizing enterocolitis;[2,16,30] spontaneous perforation of the colon, stomach, or small bowel, with or without associated smooth muscle mural defect;[1,11,17,18,19,27] ulcer disease;[17,28] and pneumatosis cystoides intestinalis.[9,10,17]

While traumatic pneumoperitoneum in infants is rare, this entity should be borne in mind by the clinician and radiologist, in the hope of reducing the high mortality in this disease spectrum.

SUMMARY

A case of perforation of the rectum by a thermometer in a premature infant with pneumoperitoneum is reported. Recent experience with 17 other cases of pneumoperitoneum in infants, and 10 cases of intestinal perforation without pneumoperitoneum, is tabulated. The mortality rate was 89 per cent in the first group and 80 per cent in the second. The literature on pneumoperitoneum and intestinal perforation in infancy is reviewed.

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A COMPLEX OF ANOMALIES ASSOCIATED WITH TRACHEOESOPHAGEAL FISTULA AND ESOPHAGEAL ATRESIA*

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ESTIMATES of the incidence of esophageal atresia and tracheoesophageal fistula range between 1 in 800 to 1 in 12,000 births with most reports showing an incidence of 1 in 3 to 4,000 births. In any case, the combination of esophageal atresia and tracheoesophageal fistula is one of the more common anomalies presenting in the immediate newborn period that requires immediate diagnosis and therapy. Moreover, in the presence of one anomaly there may well be other anomalies involving the same organ system or involving unrelated body systems. In a recent series compiled by the members of the Surgical Section of the American Academy of Pediatrics, it was found that of 1,058 patients with tracheoesophageal anomalies, 52 per cent had no associated anomalies and 48 per cent had 849 associated anomalies.[1] Congenital heart disease was the most common associated anomaly followed by gastrointestinal anomalies other than those involving the esophagus.

MATERIAL

In a review of 67 patients with esophageal atresia encountered over a period of 8 years at St. Christopher's Hospital for Children, it was found that 5 patients had a particularly significant complex of anomalies of importance from the standpoint of diagnosis and treatment. The anomalies consisted of esophageal atresia, tracheoesophageal fistula, duodenal obstruction (atresia or stenosis) and imperforate anus. Four of these 5 patients had congenital heart disease, 3 had renal anomalies, and

TABLE I

Patient	Sex	Premature or Full Term	Esophageal Atresia	Tracheoesophageal Fistula	Duodenal Obstruction	Imperforate Anus	Congenital Heart Disease	Renal Abnormality	Osseous Abnormality	Alive
JW	M	Full term	Yes	Yes	Yes Stenosis	Yes No fistula	Yes	No	No	No 5 da.
BBS	M	Premature	Yes	Yes	Yes Stenosis	Yes Rectovesical fistula	Yes	Yes Absent kidney	Yes	No 4 da.
LB	F	Premature	Yes	Yes	Yes Atresia	Yes Rectovaginal fistula	Yes	No	No	No 2 da.
LAS	F	Premature	Yes	Yes	Yes Atresia	Yes Rectovaginal fistula	Yes	Yes Ectopia	Yes	No 21 da.
NC	F	Full term	Yes	Yes	Yes Atresia	Yes Rectovaginal fistula	No	? Nonvisualization of left kidney on IVP	Yes	Yes 3 yr.

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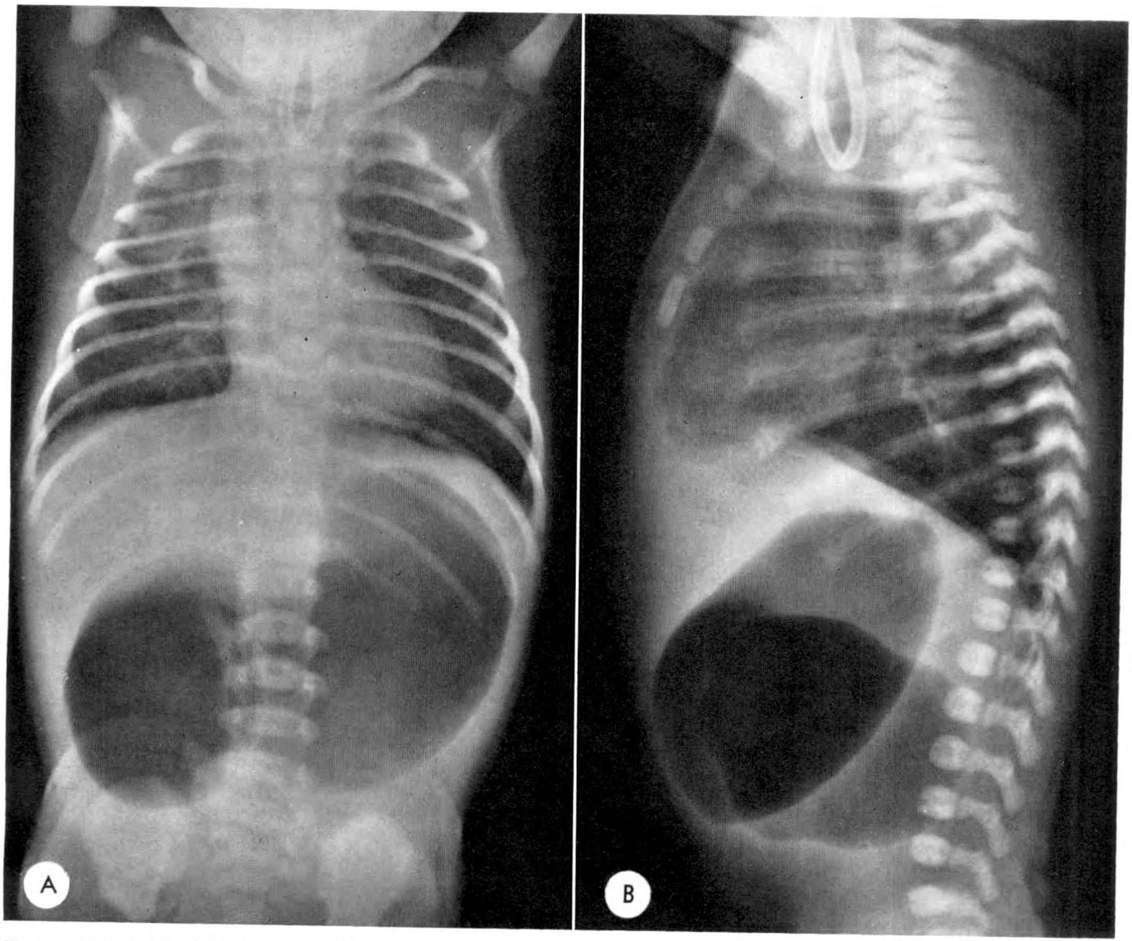

Fig 1. Patient L.B. (*A* and *B*) The roentgen examination reveals the rubber catheter coiled in the atretic esophagus. Air is evident in the stomach and also in the dilated duodenum. There is no air distal to the duodenum.

the 3 patients with renal anomalies had anomalies of the skeletal system (Table I). The osseous anomalies consisted for the most part of absence or hypoplasia of portions of the bones of the extremities, although the spine was involved in 2 patients (Table II).

CLINICAL AND ROENTGENOLOGIC FINDINGS

The clinical findings indicative of esophageal atresia have been amply described in the literature. In short, this lesion is suspected when the infant is noted to salivate excessively and become cyanotic with feedings. These symptoms may be alleviated temporarily following aspiration of the nasopharynx. The diagnosis is confirmed when it is noted that a rubber catheter cannot be passed through the esophagus and into the stomach. Roentgen examination will reveal the coiled catheter in the upper esophagus. The presence of air in the

Table II

OSSEOUS ABNORMALITIES

BBS	Hypoplasia of lumbar spine and sacrum; absent right ulna and right digits and metatarsals 3, 4, and 5 of right foot. Synostosis of toes 4 and 5 of left foot
LAS	Sprengel's deformity; anomalous ribs; bifid sacrum; absent radius and 2nd metacarpal of each hand
NC	Anomalous thumb; absent right fibula; absent 3rd metatarsal of right foot

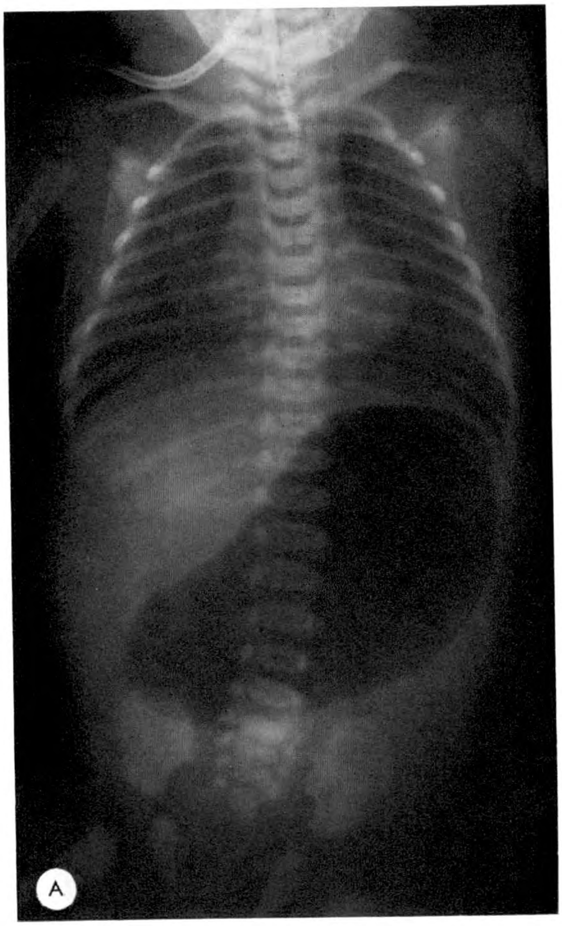

FIG. 2. Patient N.C. (*A*) The initial roentgenogram of the chest and abdomen reveals a rubber catheter in the upper esophagus and air in the distended stomach.

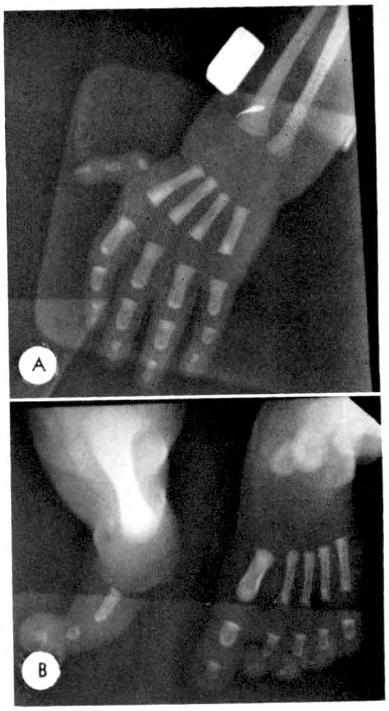

FIG. 3. Patient N.C. (*A* and *B*) Multiple osseous anomalies are evident involving the right thumb and the right foot.

stomach in the presence of esophageal atresia is evidence of a tracheoesophageal fistula. In the 5 patients of particular interest in this report, the initial roentgenograms of the chest and abdomen revealed over-aeration of the lungs with

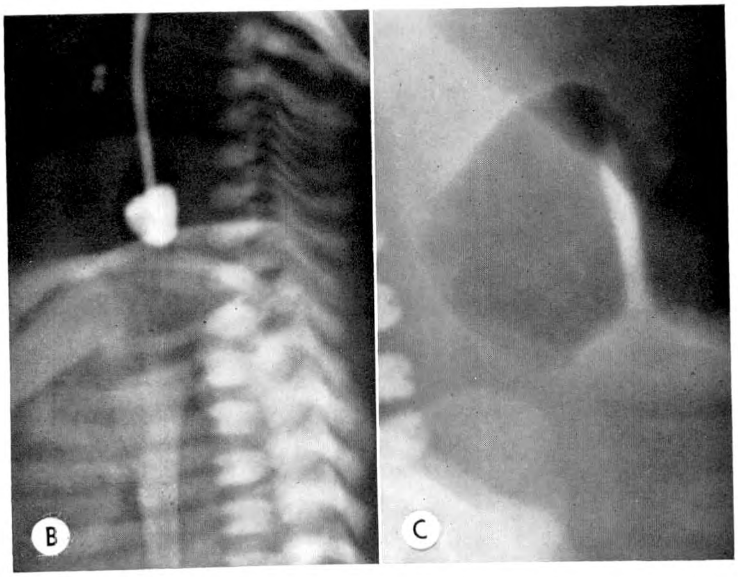

FIG. 2. Same patient. (*B*) A small amount of contrast material in the esophagus shows atresia of the esophagus. (*C*) The roentgenogram of the abdomen with the patient in the right anterior oblique position demonstrates the dilated duodenum proximal to the area of atresia in its second portion.

varying amounts of visible inflammatory exudate within them. Air was seen in the dilated upper esophageal pouch. Gas was present in the stomach. In those patients in whom duodenal atresia was present, gas was not evident distal to the duodenum (Fig. 1, *A* and *B*); in those patients in whom duodenal stenosis was present, the duodenum and the stomach were dilated but gas was evident distal to the dilated duodenum. When the dilated duodenum was filled with fluid, it was possible by positioning the patient on the roentgenographic table to displace the fluid from the duodenum and to displace air into the duodenum so that the obstructive phenomenon was readily visualized (Fig. 2, *A*, *B* and *C*). The patient with esophageal atresia, tracheoesophageal fistula, and duodenal obstruction may vomit bile-stained material, the material going up the esophagus, through the fistula, into the trachea and hence into the pharynx and mouth.

The imperforate anus in these patients was apparent upon inspection of the perineum. Fistulas from the rectum to the perineum are usually evident by inspection of the perineum; at times, fistulas to the bladder or vagina are identified by roentgen examination utilizing the injection of contrast material into the vagina or the urethra or the urinary bladder.

Two of the 3 patients who had renal abnormalities did not survive, the abnormality being found at postmortem study. In one patient the kidneys were absent, in the other a fused pelvic kidney was present. In the third patient positive proof of renal abnormality was not present; however, at the time of intravenous urography only one collecting system was visualized. All patients with renal anomalies also had osseous abnormalities (Fig. 3, *A–D*).

SUMMARY

Five patients with a complex of anomalies associated with esophageal atresia and tracheoesophageal fistula have been described. The recognition of this complex of anomalies is of significance in diagnosis and treatment. The relationship between the renal abnormalities and the osseous abnormalities is not apparent. The grave prognosis associated with this complex is evident by the fact that but 1 of the 5 patients is surviving.

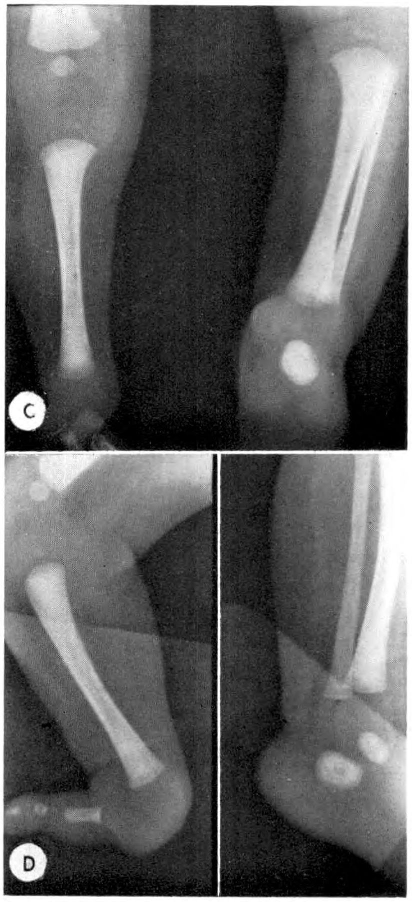

FIG. 3. Same patient. (*C* and *D*) Involvement of the right lower extremity as compared to the normal left lower extremity.

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VIDEO TAPE RECORDING IN THE DIAGNOSIS OF TRACHEO-ESOPHAGEAL FISTULA WITHOUT ESOPHAGEAL ATRESIA*

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ONLY rarely (3–10 per cent) is congenital tracheobronchial fistula not accompanied by esophageal atresia[3,4] and not only is the condition rare but also difficult to diagnose.[1,3] It does not suffice merely to demonstrate contrast material administered by mouth in the trachea because it is commonplace for infants to regurgitate and then aspirate during the course of a roentgenologic examination.

To avoid misinterpreting such regurgitation as fistula, it is necessary that the examiner see fluoroscopically the actual transit of the medium from the esophagus through an abnormal passageway into the trachea and highly desirable that he record it as well on the roentgenogram. In those cases where a fistula actually does exist, an experienced and patient examiner usually will be able to detect it, at least fleetingly, during the course of fluoroscopy, but it always is difficult and sometimes impossible for him to synchronize conventional spot roentgenography with the brief spurts of contrast material.

When video tape apparatus is available, the entire fluoroscopic examination can be recorded without additional cost or radiation hazard and, when such a tape is played back, it provides convincing support for the fluoroscopic report. It might be asked whether cine film would be superior to tape for such continuous recording, but at present, this is impractical. Added dose could be avoided, it is true, by filming from a kinescope rather than directly from the phosphor of the image tube, but the reels of present day roentgen-ray cine cameras hold far too little film for such work, and, even if they were to be made larger, there would remain the excessive cost of the long film strips required for the protracted examinations sometimes necessary for the demonstration of such fistulas.

REPORT OF A CASE

An 8 month old girl had coughed since birth and on admission was found to have pneumonic consolidation of the right upper lung lobe. At the age of 6 weeks, roentgenograms of the esophagus had been reported as normal but at the age of 3 months there was questionable roentgenographic evidence of tracheobronchial fistula. Shortly before admission to our hospital, a roentgenogram showed barium in both the esophagus and the trachea, with highly suggestive evidence of a small caliber fistula extending anteriorly from the mid-esophagus, presumably communicating with the trachea.

For our roentgenologic examination the infant was placed, right side down, on the surface of a fluoroscopic table, tilted into a slightly "head down" position, and a polyethylene catheter was passed through the nose into the esophagus and advanced until its tip lay at about the middle of the esophagus. Under fluoroscopic control (monitored continuously by video tape), diatrizoate (hypaque 50 per cent) was injected slowly through the catheter.

At the first injection no fistula could be seen and, when the esophagus was about half filled with medium, the infant swallowed, causing the contrast material to pass into the stomach. At the second injection filling was more complete before swallowing occurred but still no fistula was demonstrated. At the third attempt esophageal filling had reached to about the level of the carina when, with a convulsive effort, the infant swallowed vigorously and some of the contrast medium was seen to spurt through a fine caliber fistula, extending superiorly and anteriorly to communicate with the trachea. As soon as the material entered the trachea, coughing was induced. This resulted in the spread of the hypaque throughout the bronchial tree, the entire sequence occurring so rapidly that it was impossible to record it on spot or cine film. These events were captured by video tape, however, which subsequently was played back for surgeons and other interested physicians. At surgery, the fistula, measuring 2 mm. in diameter, was located and excised.

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SUMMARY

A case is presented in which a diagnosis of a tracheo-esophageal fistula in an 8 month old patient was made by employing video tape recording. Its advantages are discussed.

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MECONIUM ILEUS

DEMONSTRATION OF THE MECONIUM MASS ON BARIUM ENEMA STUDY

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MECONIUM ileus is one of the complications of mucoviscidosis (fibrocystic disease), occurring in the neonatal period.[2,3,4,13] The inspissated mass of viscid meconium produces low small bowel obstruction with a roentgen picture of diffuse small bowel dilatation. The following signs have been described to help differentiate meconium ileus from obstruction due to ileal atresia or stenosis.

1. The loops of gas filled bowel vary greatly in size; some are enormously ballooned out, others are only moderately enlarged, some may be rather normal in size and some even somewhat smaller than expected normal.[7]

2. There is a mottled appearance of the distal intestinal contents due to minute bubbles of gas mixed in the tenacious meconium.[11]

3. Fluid levels are absent or few in number in the upright roentgenograms.[12,14]

4. Abdominal calcifications are noted if there has been antenatal small bowel perforation with escape of meconium into the peritoneal cavity. This sign is not specific since it may be present secondary to other causes of perforation.[6]

The barium enema study has been considered useful in showing the presence of a colon of markedly reduced caliber but of normal length (unused colon or microcolon), thus proving that the dilated loops are small bowel.[6,15] It has not previously been reported to be of any value in elucidating the cause of the low small bowel obstruction.

We recently studied a case of meconium ileus in which the barium enema study with retrograde filling of the distal ileum demonstrated the features of the inspissated meconium mass, thus further proving the diagnosis.

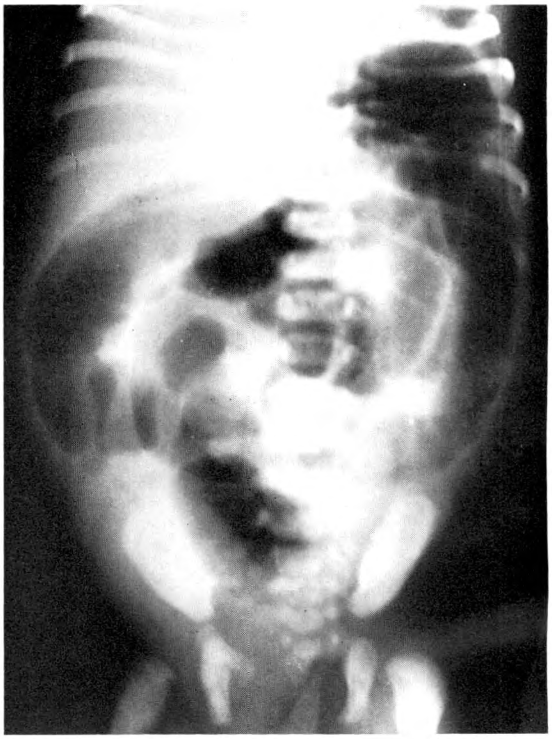

FIG. 1. Erect abdominal roentgenogram showing multiple dilated gas filled loops of bowel of varying sizes but with few air fluid levels.

REPORT OF A CASE

This newborn female infant was the product of a normal full term gestation and delivery. During the first 2 days of life no meconium was passed and the abdomen became progressively distended. On the second day of life green emesis also occurred.

Roentgen examination of the abdomen on the second day of life showed diffuse small bowel dilatation. There was variation in the size of the loops with a number of hugely dilated loops. Fluid levels were relatively few in the erect roentgenograms (Fig. 1). A barium enema study showed a colon of markedly reduced caliber but of normal length and position. Barium passing into the distal ileum filled the ileum for a distance of about 20 cm. and demonstrated a gradual increase in its caliber from the ileocecal valve to the point of obstruction. At this point, the ileum was considerably dilated and showed an elongated intraluminal filling defect due to the meconium mass, coated on its surface by the barium. There was telescoping of the bowel over the meconium mass. The barium did not fill any of the gas filled loops (Fig. 2 and 3).

Operation was performed and the diagnosis of meconium ileus was confirmed. Because of the thick rubbery nature of the meconium, it was impossible to remove it from the ileum and, therefore, 45 cm. of ileum was resected with the distal line of resection about 30 cm. proximal to the ileocecal valve. The remainder of the bowel was cleansed and a T anastomosis and venting ileostomy were performed.

Pathologic study of the small bowel specimen showed the lumen to be filled with tenacious meconium (Fig. 4). Microscopic examination showed muscular hypertrophy.

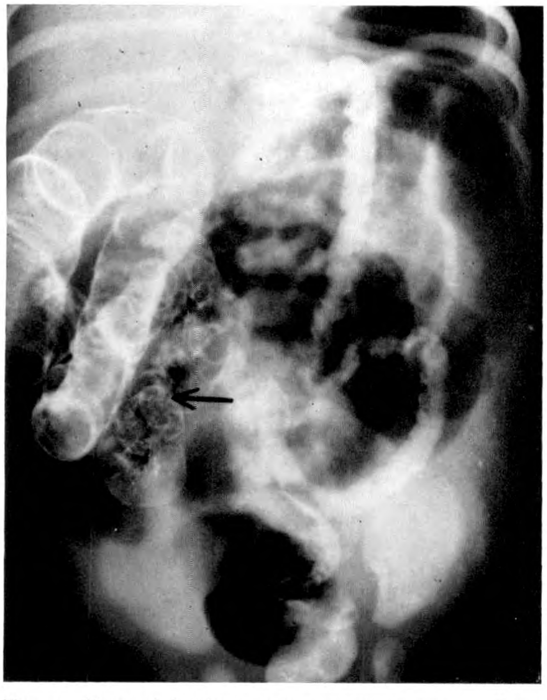

Fig. 2. Frontal barium enema roentgenogram demonstrating a colon of markedly reduced caliber but of normal length. The cecum (arrow) is in normal position. The ileum is opacified and shows a gradual increase in caliber to the point of obstruction. It contains an elongated filling defect due to the mass of meconium.

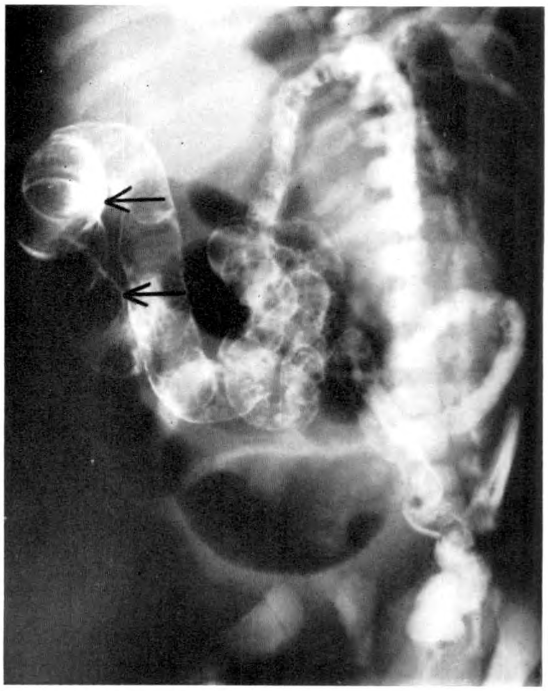

Fig. 3. Oblique barium enema roentgenogram demonstrating telescoping of the dilated ileum over the meconium mass (arrows).

DISCUSSION

No previous report specifically mentions the demonstration of the small bowel in meconium ileus by retrograde barium study. This is probably related to the tenacious secretions agglutinating the walls of the unused colon and causing difficulty in barium filling.[1,5] The examiner is usually satisfied with demonstration of the microcolon proving the presence of small bowel obstruction and does not attempt to demonstrate the small bowel. Although in the reported study no planned attempt was made to fill the small bowel, its demonstration produced a definitive diagnosis of meconium ileus. Further attempts in sim-

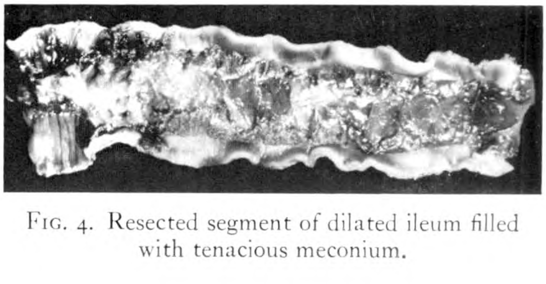

Fig. 4. Resected segment of dilated ileum filled with tenacious meconium.

ilar cases thus appear worthwhile.

The appearance of the small bowel at surgical exploration is fairly characteristic.[8,9,10] A segment of terminal ileum which varies from 20 to 40 cm. in length is collapsed and filled with hard grayish white concretions which make a perfect cast of its inside. Proximally, the ileum is distended over a variable distance with heavy thick green black meconium. The area of maximum hypertrophy and dilatation is in the mid-ileum, which will often measure up to 7 cm. in diameter.

The roentgen features of the distal portion of the inspissated meconium mass, as noted in the reported case, are those of an elongated smooth filling defect causing obstruction to the retrograde flow of barium. The ileum which is dilated at this site tapers distally with reduced caliber in its distal portion for the few centimeters proximal to the ileocecal valve. At the site of obstruction, it telescopes over the intraluminal mass, producing the "coil spring" appearance noted with intussusception.

SUMMARY

A case of meconium ileus is reported in which a barium enema study with retrograde filling of the ileum demonstrated the inspissated meconium mass. The roentgen appearance is that of an elongated smooth intraluminal filling defect with telescoping of the bowel over it at the site of obstruction in the mid-ileum.

This finding apparently represents a specific roentgen sign of meconium ileus.

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ROENTGENOLOGIC MANIFESTATIONS OF HIRSCHSPRUNG'S DISEASE IN INFANCY*

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HIRSCHSPRUNG'S disease is a potentially lethal congenital anomaly with a high attrition rate in infants. In 1948 Zuelzer and Wilson,[6] and Whitehouse and Kernohan[5] reported the pathogenesis of this disease as an absence of the ganglion cells of the myenteric plexus in a segment of bowel. In 1949 when Swenson, Neuhauser, and Pickett[4] described the clinical and roentgen method of diagnosis of Hirschsprung's disease, the whole question of megacolon resolved itself into a differentiation between a relatively small group of constipated children with true aganglionosis (Fig. 1, *A* and *B*) and a much larger group of constipated children with no demonstrable organic lesion of the bowel, designated as functional chronic constipation (Fig. 2, *A* and *B*). For a number of years the main problem in the Philadelphia area, and in other large metropolitan areas, resolved itself into a gradual separation of patients with the true aganglionic Hirschsprung's disease from the vast majority of older, chronically constipated children. Little by little this separation has taken place, and today most of the older children with aganglionosis have been operated upon, while those with functional chronic constipation have hopefully found their way to competent medical management. It would be wrong to say that we never see the classic pot-bellied, emaciated, undersized older child with true Hirschsprung's disease any longer, because upon rare occasion a neglected child still turns up (Fig. 3, *A*, *B* and *C*), but for the most part the problem has moved back into a younger age group. During the years when we were learning how to make the diagnosis and correct the problem in older children, the infants were going unrecognized and some were dying.

True aganglionosis of the bowel, as with most diseases, falls into a spectrum ranging from severe forms, to less severe, to mild, to equivocal. This is not just a matter of the length of the aganglionic segment, but sometimes, given two babies with the same amount of bowel involved, one may be completely obstructed, while the other is only slightly obstructed. Perhaps this is a matter of degree of aganglionosis. Whatever the true explanation, the older child diagnosed with the disease obviously survived infancy, but at the same time other babies with the more severe forms of the disease were dying early of intestinal obstruction. Little by little, therefore, it has behooved us to learn how to make the diagnosis earlier.

SYMPTOMATOLOGY

Ordinarily, one considers constipation as the chief symptom of Hirschsprung's disease. This is true in the older child who has survived infancy. However, in the newborn and for several months after birth, constipation is seldom the presenting symptom. A significant percentage presents as neonatal bowel obstruction, as fulminating gastroenteritis, and as chronic diarrhea with failure to thrive, the latter with protein-losing enteropathy as the extreme. If demonstration of the transition zone, that is, an abrupt change in caliber between the ganglionic and aganglionic bowel, be required for diagnosis, a certain number of the affected infants will not be diagnosed.

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THE DILEMMA OF THE TRANSITION ZONE IN INFANCY

The distal aganglionic segment is not truly contracted or strictured, but is relatively narrow as compared to the proximal dilated bowel. The distal segment can be passively dilated by impacted stool as well as by repeated enemas and rectal manipulations required to remove the impactions (Fig. 4, *A* and *B*). This passive dilatation of the aganglionic segment may occur to such a degree that a significant portion of the proximal (cephalic) dilated bowel may be aganglionic. Therefore, a short distal segment may be obliterated by this phenomenon and may be difficult to demonstrate. Under these circumstances, rectal biopsy is necessary for diagnosis.

The proximal dilatation of the normal bowel is a compensatory change as a result of the obstruction produced by failure of the distal aganglionic segment effectively to propel its contents distally. The change can be absent in the early neonatal period. Liquid and soft stool can be propelled through the afunctional segment, and, as long as the stool is soft, effective emptying of the colon can occur and proximal dilatation is not seen. In the rare case of involvement of the entire colon, a transition zone does not exist (Fig. 5, *A* and *B*).

Therefore, in infants, the distal segment may not only be relatively wide, but the proximal segment may not as yet be dilated. In addition, we have found two conditions which mimic a transition zone.

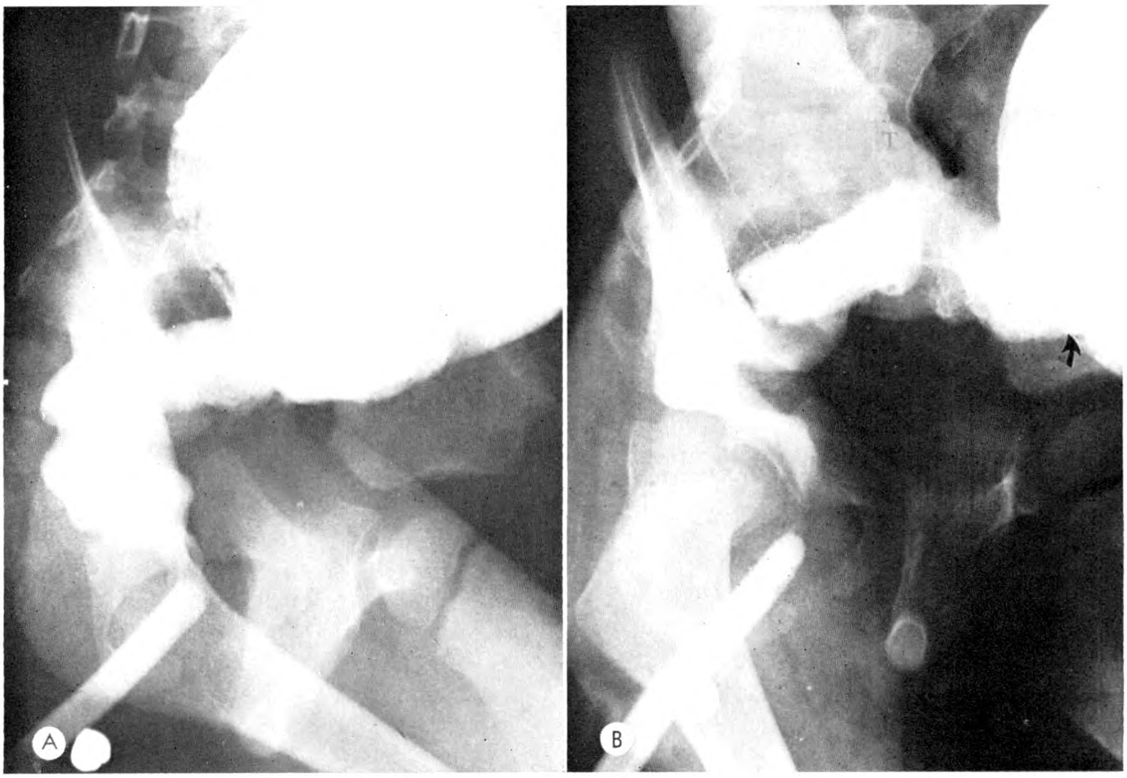

Fig. 1. A 3 year old male constipated since birth. (*A*) Oblique spot roentgenogram of a barium enema study taken during fluoroscopy. Note the tip of the enema tube only 1 inch in from the mucocutaneous line (lead marker). A terminal aganglionic segment is visualized, but the zone of demarcation is overlapped. (*B*) Oblique spot roentgenogram with a little less obliquity shows the zone of demarcation (arrow). The diagnosis of Hirschsprung's disease is obvious.

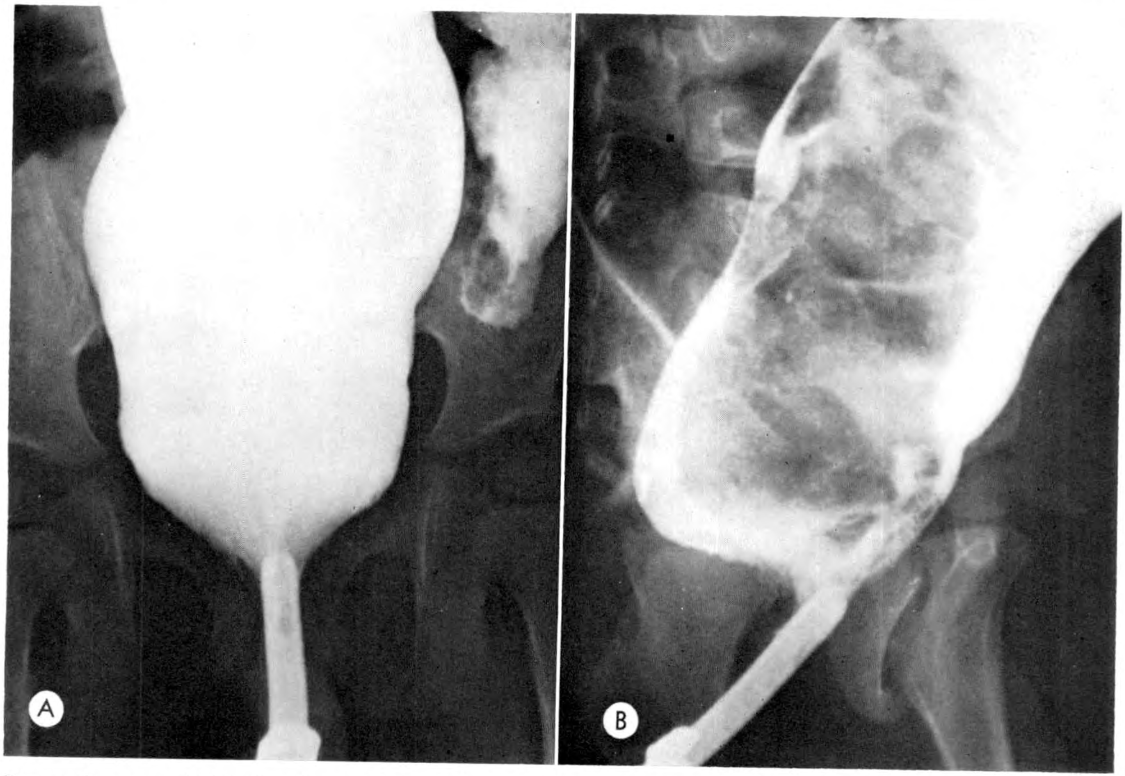

Fig. 2. A 3 year old blind male constipated since birth. (*A*) Anteroposterior spot roentgenogram of a barium enema study taken during fluoroscopy. Again, note the tip of the enema tube to be only 1 inch in from the mucocutaneous line. The rectum "balloons" from immediately inside the internal sphincter. (*B*) Oblique spot roentgenogram of the pelvis taken during fluoroscopy. This view demonstrates the huge widening of the rectum beginning just inside the internal sphincter. Also, note the large bolus of feces filling the rectum. This is a classic picture of functional chronic constipation.

Both are rare, but each certainly adds to the dilemma. Seven infants examined in the first week of life because of abdominal distention and absence of bowel movements have shown a dilated ascending and transverse colon and a narrow descending colon and sigmoid. The zone of transition took place in the region of the splenic flexure (Fig. 6, *A* and *B*). The narrowed distal portion was smooth and of uniform diameter all the way to the anus. We interpreted the first 2 of these 5 as true Hirschsprung's disease. The first came to autopsy and had ganglion cells all through the bowel. The second was operated upon and had a transverse colostomy with biopsies along the narrowed descending colon and sigmoid. All biopsies showed ganglion cells. The colostomy was subsequently closed and the child developed normal bowel habits. A follow-up barium enema examination at 2 years revealed a normal colon. Because of these 2 cases, we became somewhat wary, and in the absence of the pathognomonic signs which will be discussed, we simply observed the next 5 infants. Each child has turned out to have a normal bowel with normal bowel habits. It therefore seems possible that, in each case, we have been dealing with Cannon's ring at the level of the splenic flexure, rather than at its usual position in the proximal transverse colon.

The other confusing entity is an extraperitoneal pelvic abscess narrowing the rectum by extrinsic pressure. The clinical picture of sepsis and toxicity may help in differentiation, but can also occur in the extremely ill child with Hirschsprung's disease. A most helpful finding, if present, is edema of the legs and venous obstruction in

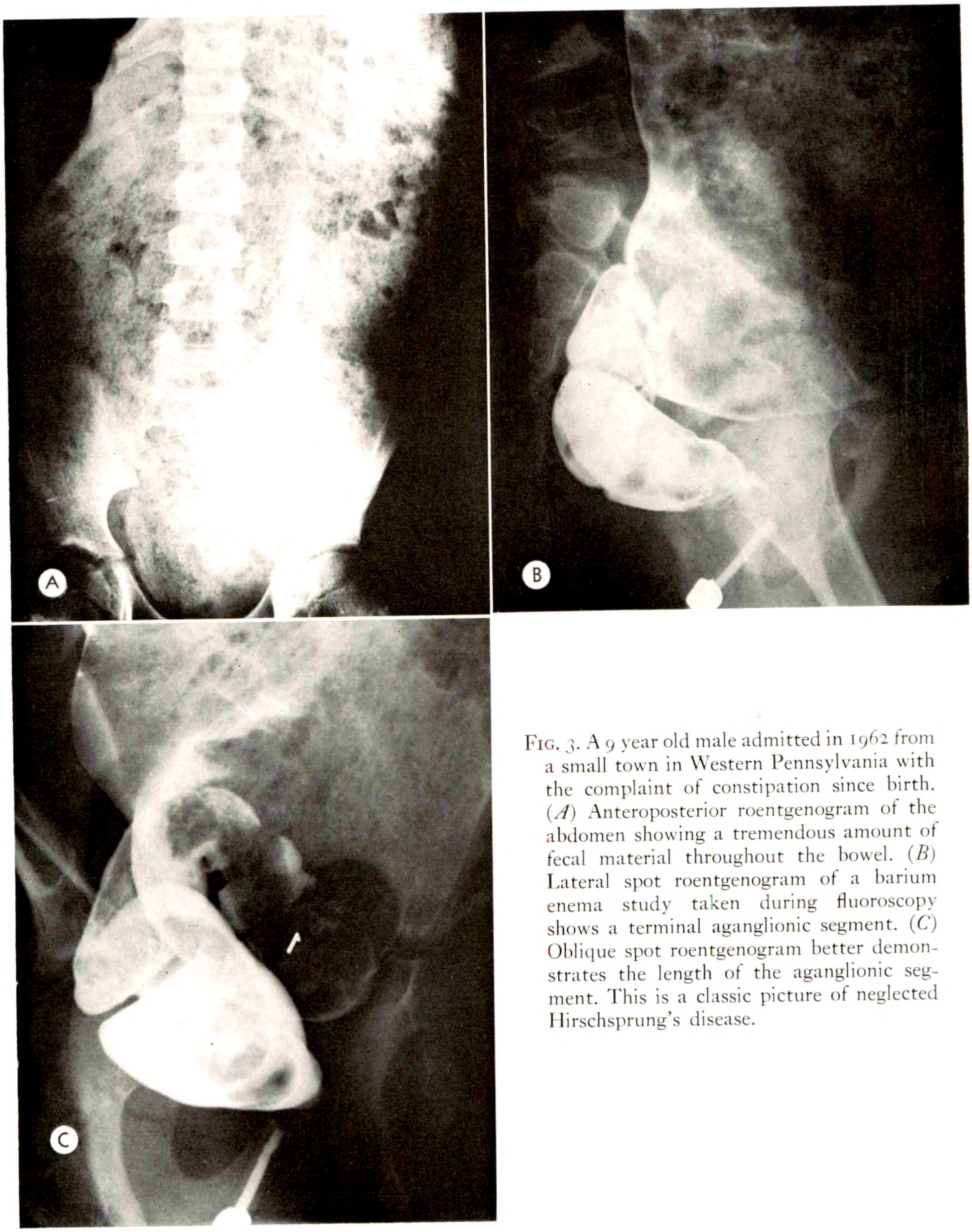

FIG. 3. A 9 year old male admitted in 1962 from a small town in Western Pennsylvania with the complaint of constipation since birth. (*A*) Anteroposterior roentgenogram of the abdomen showing a tremendous amount of fecal material throughout the bowel. (*B*) Lateral spot roentgenogram of a barium enema study taken during fluoroscopy shows a terminal aganglionic segment. (*C*) Oblique spot roentgenogram better demonstrates the length of the aganglionic segment. This is a classic picture of neglected Hirschsprung's disease.

the presence of a pelvic abscess.

To date, at The Children's Hospital of Philadelphia, there has been no case of a so-called "skip area" of aganglionosis. Before we appreciated the fact that excessive parental manipulation may dilate the rectum, we thought that we had demonstrated several such cases by barium enema

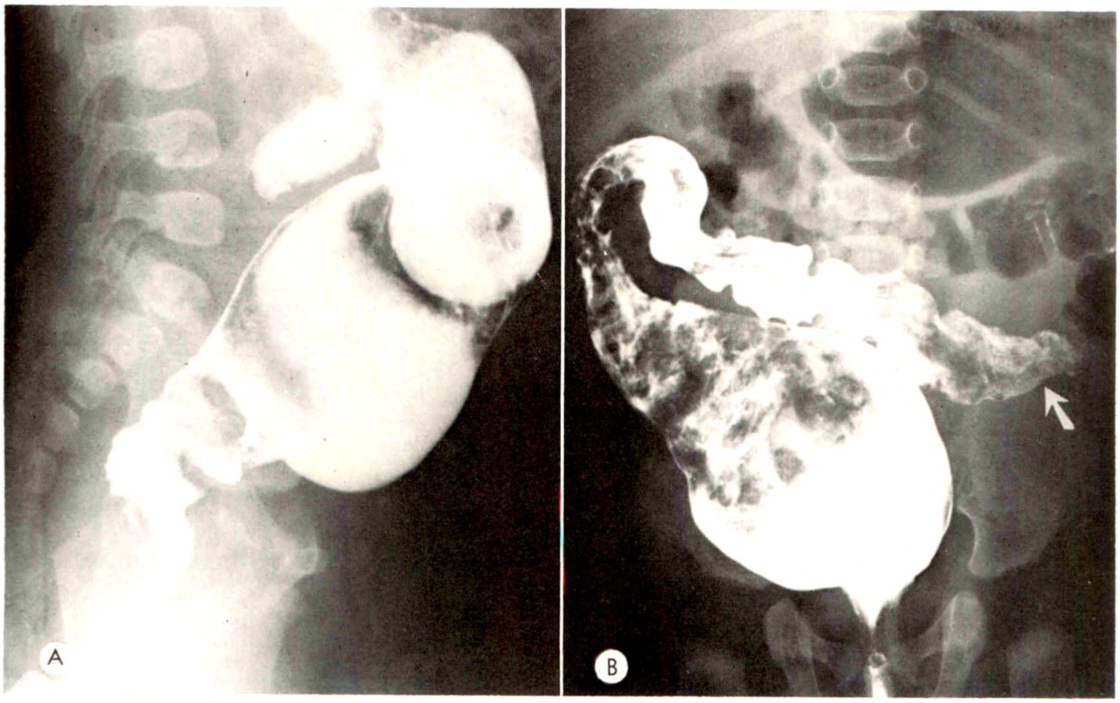

Fig. 4. A 6 month old male constipated since 2 months of age. (*A*) Lateral spot roentgenogram of a barium enema study taken during fluoroscopy shows a rectum apparently of normal diameter with a disproportionate dilatation beginning at the rectosigmoid. (*B*) Anteroposterior roentgenogram of a barium enema study shows a redundant sigmoid with a huge bolus of fecal material lodged at the rectosigmoid. Irregular, bizarre contractions of the entire sigmoid extend to the descending colon (arrow). Pathologic examination revealed aganglionosis extending throughout the entire rectum and sigmoid. This case shows how impacted stool may passively dilate the aganglionic segment. The irregular, bizarre contractions of the entire sigmoid demonstrate the extent of the aganglionosis.

examination, but the biopsies always showed the aganglionosis to extend to the anal area.

PATHOGNOMONIC ROENTGEN SIGNS IN INFANCY

1. ZONE OF TRANSITION

The most diagnostic and reliable roentgen finding is a well demarcated zone of transition between the aganglionic distal segment and the normal ganglionic proximal segment. For reasons already discussed, such a clear-cut zone is not always present at birth, but when present, the diagnosis is relatively simple (Fig. 7, *A* and *B*).

2. IRREGULAR, BIZARRE CONTRACTIONS OF AGANGLIONIC SEGMENT

In the absence of a diagnostic transitional zone, we have come to rely upon a pattern of irregular contractions in the aganglionic segment (Fig. 8, *A–D*). In many of the articles already written on the subject of Hirschsprung's disease, various illustrations have shown these irregular contractions, but we have not found them described as a diagnostic sign. The first time we recognized them consciously, we described them as large, irregular saw teeth. These indentations are irregular in both spacing and extent, and do not circle the bowel. Their chief diagnostic feature is their irregularity. They are apparently the result of the dysrhythmia produced by the aganglionosis. In infants, these irregular contractions of the aganglionic segment are a more frequent finding than is a well-demarcated transitional zone. As already shown in Figure 5, *A* and *B* they were the only clue when the entire colon was in-

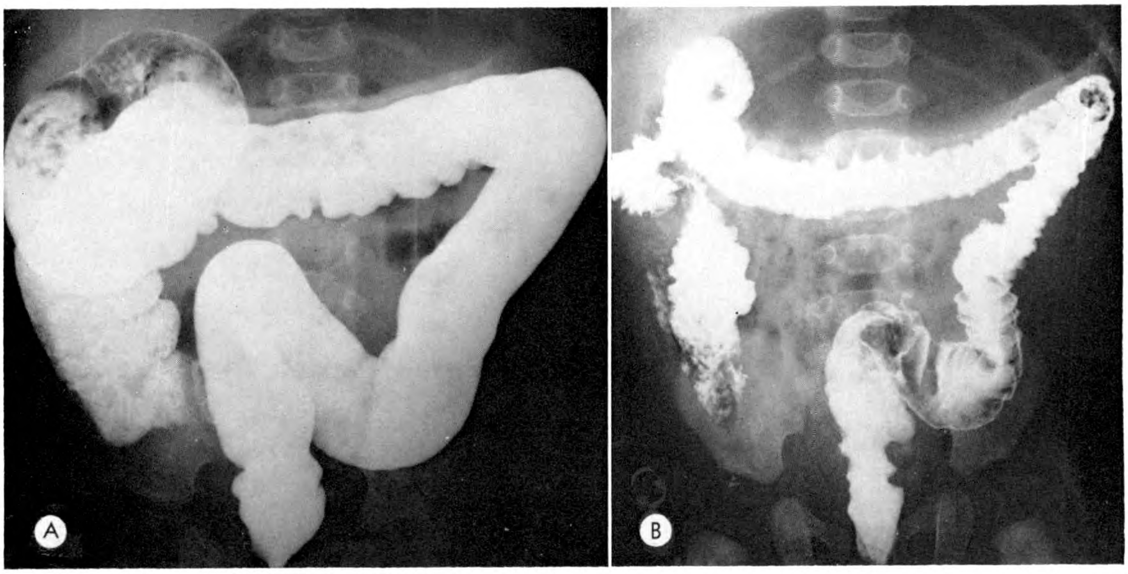

FIG. 5. A 3 month old male with a history of alternating diarrhea and constipation. There was a family history of Hirschsprung's disease in other siblings. (*A*) Anteroposterior roentgenogram of the barium-filled colon showing an apparently normal colon. (*B*) Anteroposterior roentgenogram of the colon after evacuation shows peculiar, irregular, bizarre, "sawtoothed" contractions of the entire colon. Pathologic examination revealed aganglionosis involving the entire colon. If it had not been for the family history of Hirschsprung's disease, the diagnosis would probably have been missed. The case illustrates the significance of the irregular, bizarre contractions of the aganglionic segment which are often best visualized on the postevacuation roentgenogram.

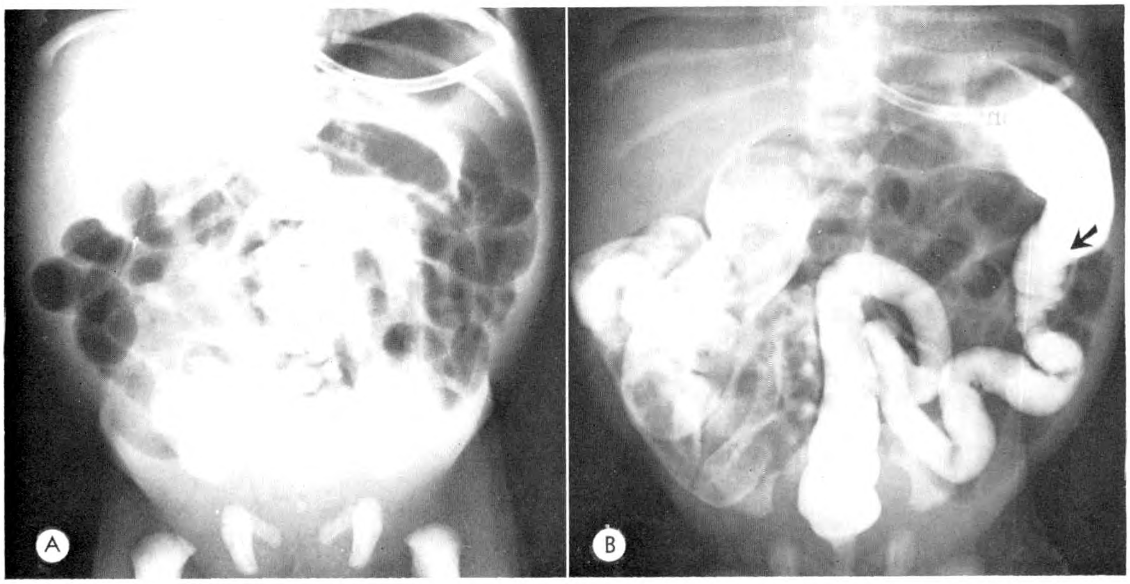

FIG. 6. A 2 day old male admitted because of abdominal distention and absence of bowel movements. (*A*) Anteroposterior roentgenogram of the abdomen showing moderate distention of the bowel. Whether this is only small bowel, or a combination of small and large bowel, cannot be determined. (*B*) Anteroposterior roentgenogram of the barium-filled colon reveals a zone of demarcation between a relatively narrow distal large bowel and a moderately dilated proximal large bowel (arrow). Note, however, the uniform character of the narrowed segment with no irregular, bizarre contractions. The baby was simply observed, and began to stool on the fourth day of life and has been normal since that time.

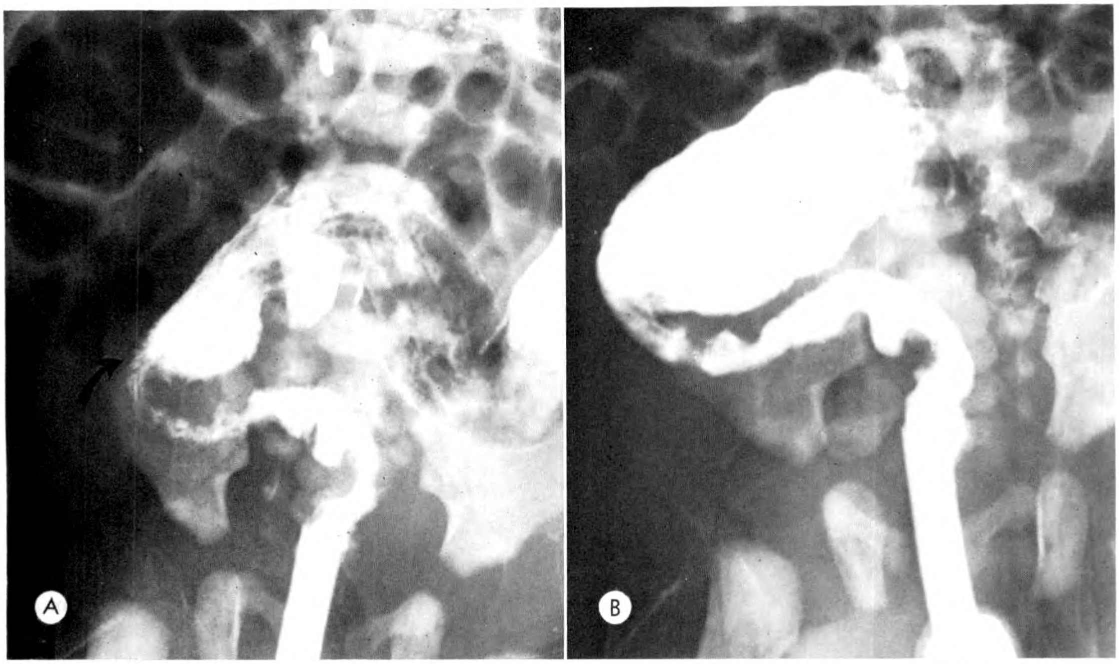

Fig. 7. A 48 hour old male with abdominal distention and absence of bowel movements. (*A*) Anteroposterior spot roentgenogram taken during the early phase of a barium enema examination showing an apparent zone of demarcation (arrow). (*B*) Anteroposterior spot roentgenogram taken after the introduction of more barium showing a definite zone of demarcation. Note in both roentgenograms the irregular, deep, bizarre contractions in what proved to be an aganglionic segment.

volved. In the case of a large bolus of feces working itself into the aganglionic segment and producing a confusing dilatation, these irregular contractions revealed the true extent of the aganglionosis (Fig. 4, *A* and *B*). The importance of these bizarre contractions is further emphasized in the 7 normal infants already discussed, with a zone of transition near the splenic flexure. As shown in Figure 6, *A* and *B*, the distal bowel is of a uniform width, showing none of these irregular contractions. This was true in all 7 of these infants. The absence of these bizarre, irregular contractions certainly militates against the presence of an aganglionosis.

3. BARIUM RETENTION FOLLOWING A BARIUM ENEMA STUDY

In 1957 Evans and Willis[1] discussed the importance of barium retention 24 and 48 hours after a barium enema study as a diagnostic sign in infants with Hirschsprung's disease. It is true, as Neuhauser first pointed out in 1949, that in the presence of a transition zone one should not fill the entire colon with barium. However, Evans and Willis were discussing the infant who lacks a clear-cut zone of transition. We also have become impressed with the value of the 24 and 48 hour delayed roentgenogram. Evacuation of the barium enema may be almost complete because the proximal normal bowel contracts forcefully enough to propel the liquid enema through the abnormal distal segment. At 24 hours a small amount of barium remaining is often seen mixed uniformly through the colon, and the pathophysiology of the disease becomes apparent as the formed feces collect behind the aganglionic segment (Fig. 9, *A*, *B* and *C*). In chronic constipation, and in normal children, the retained barium is usually collected as boli in the rectum and sigmoid. The uniform mixing of the barium through the bowel followed by prolonged retention, even for weeks (Fig. 10, *A* and *B*), is an objective demonstration of the

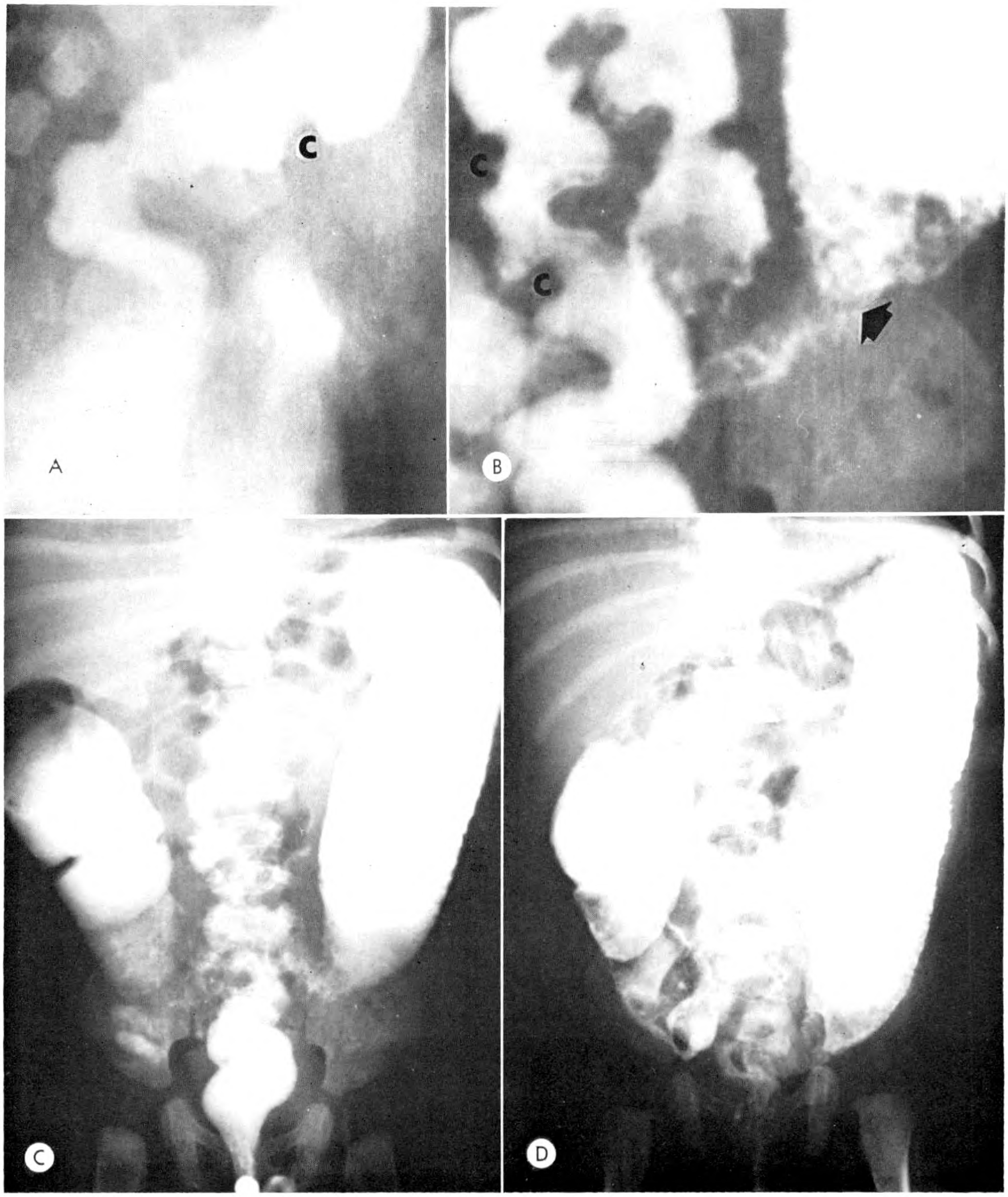

FIG. 8. A 2 month old female with constipation and abdominal distention. (*A*) Lateral spot roentgenogram taken at the beginning of a barium enema examination showing one deep, irregular contraction (C) in what proved to be an aganglionic rectum. (*B*) Anteroposterior spot roentgenogram taken after the introduction of more barium showing a zone of demarcation (arrow), and a number of deep, irregular, bizarre contractions (C) in the distal aganglionic segment. (*C*) Anteroposterior roentgenogram of the colon showing fine serrations produced by transverse parallel folds proximal to the zone of demarcation. (*D*) Anteroposterior roentgenogram taken after evacuation better demonstrates the fine serrations produced by the transverse parallel folds of the colon proximal to the zone of demarcation.

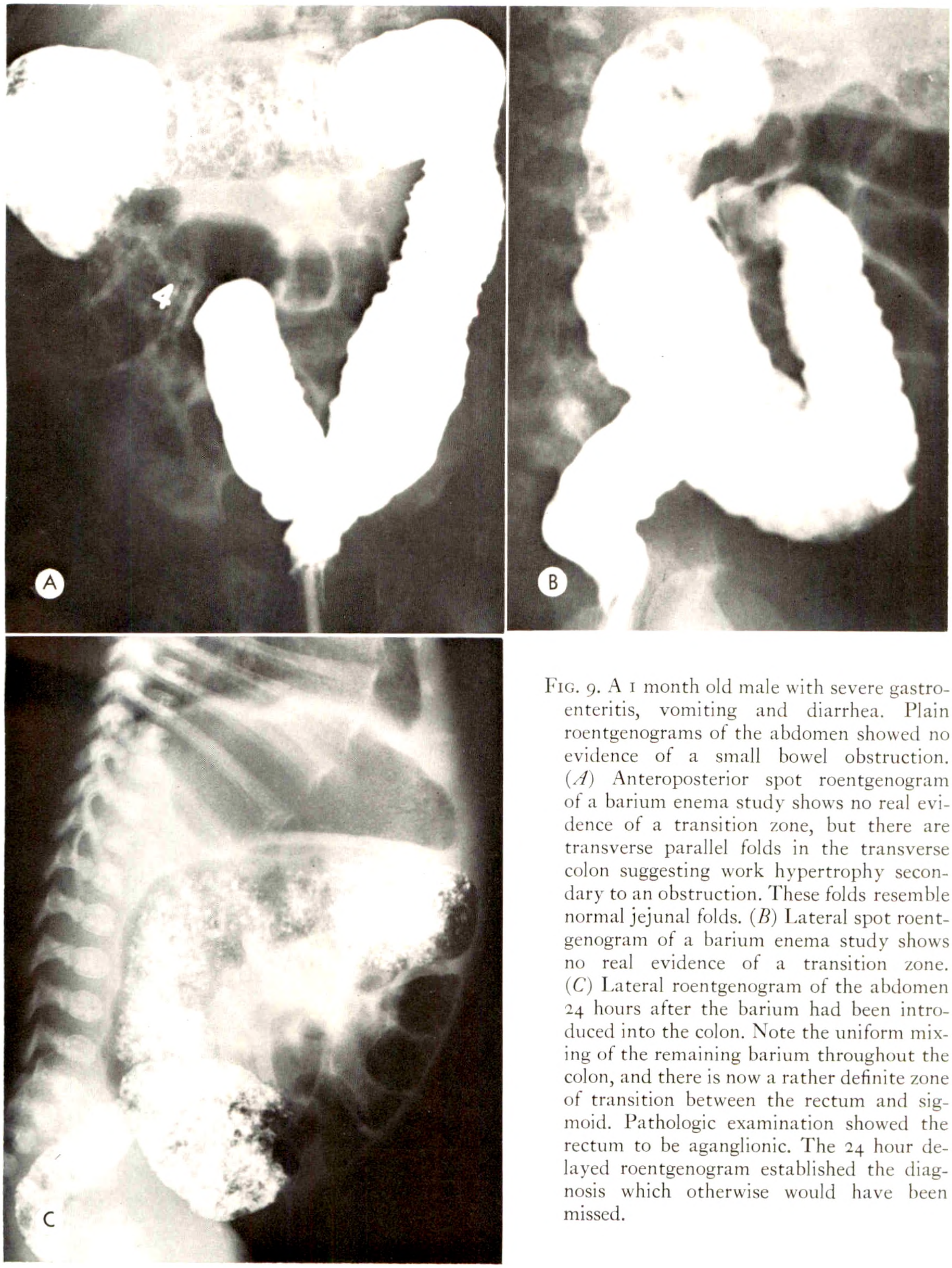

FIG. 9. A 1 month old male with severe gastroenteritis, vomiting and diarrhea. Plain roentgenograms of the abdomen showed no evidence of a small bowel obstruction. (*A*) Anteroposterior spot roentgenogram of a barium enema study shows no real evidence of a transition zone, but there are transverse parallel folds in the transverse colon suggesting work hypertrophy secondary to an obstruction. These folds resemble normal jejunal folds. (*B*) Lateral spot roentgenogram of a barium enema study shows no real evidence of a transition zone. (*C*) Lateral roentgenogram of the abdomen 24 hours after the barium had been introduced into the colon. Note the uniform mixing of the remaining barium throughout the colon, and there is now a rather definite zone of transition between the rectum and sigmoid. Pathologic examination showed the rectum to be aganglionic. The 24 hour delayed roentgenogram established the diagnosis which otherwise would have been missed.

stasis occurring in Hirschsprung's disease. This information is at times helpful in equivocal cases, but is lost if a water-soluble contrast material is used. At times, there may be a disproportionate dilatation of the sigmoid in the presence of a rectum of normal caliber and in the absence of dilatation of the rest of the colon. The dilatation of the sigmoid is extreme enough to be questionably abnormal. The common denominator in this group is that these children have been subjected to determined efforts to obtain regular and frequent bowel movements, and these efforts have been effective. This is the picture of satisfactory medical management of Hirschsprung's disease. These cases seldom show a transition zone because the distal segment has been passively dilated by the mothers' efforts. However, this group has barium retention at 24 hours in the dilated sigmoid. If the enemas are not continued, the full-blown transition zone appears. This group will not be found in the immediate neonatal period, but in the child old enough to have had considerable parental manipulation.

4. PARALLEL TRANSVERSE FOLDS IN THE DILATED PROXIMAL COLON

Frequently, in infantile Hirschsprung's disease there is a pattern of smooth, parallel, transverse folds in the overworking proximal colon. These folds in the proximal colon resemble normal jejunal folds. They are the result of work hypertrophy and can occur proximal to any partial obstruction, but are almost nonexistent in the normal colon. Twice we have seen these folds in what proved to be normal colons, but in

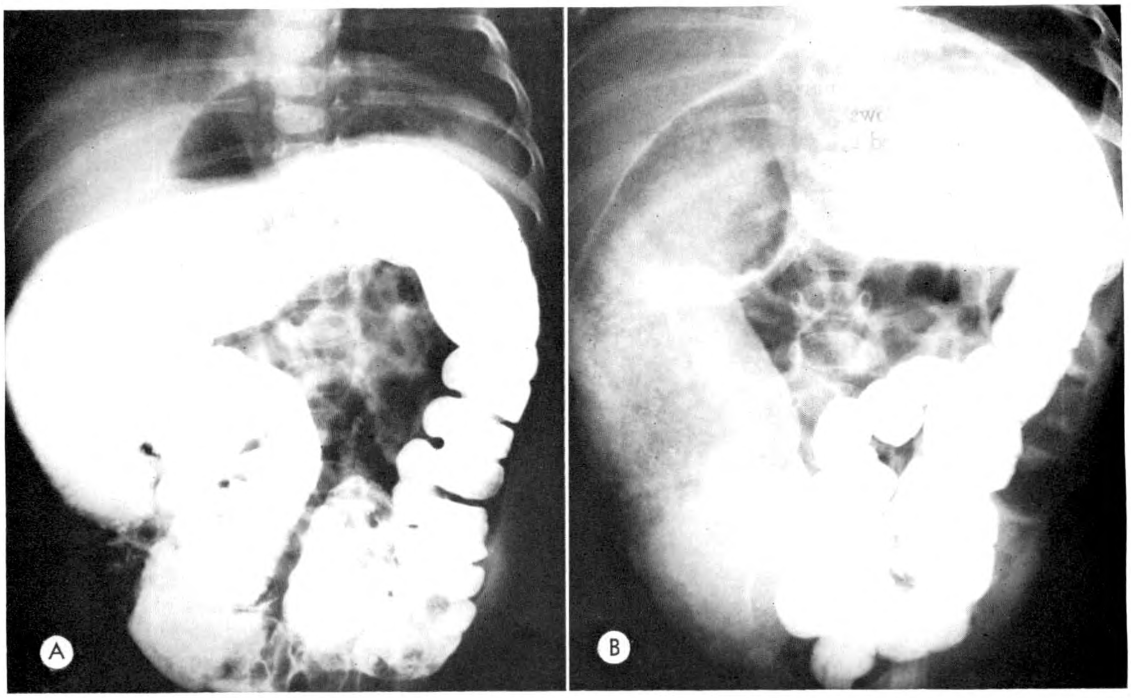

Fig. 10. A 2 month old male admitted because of abdominal distention, vomiting and diarrhea. Plain roentgenograms of the abdomen revealed a paravertebral soft tissue mass on the right side extending from D6 to D12. This proved to be a neuroblastoma. (*A*) Anteroposterior roentgenogram of a barium enema study showing a dilated proximal colon and a narrower distal colon. There is no clear-cut zone of demarcation. There are vague, parallel, transverse folds in the proximal colon. (*B*) Anteroposterior roentgenogram of the abdomen taken 10 days after the barium was first introduced. Note the uniform mixing of the retained barium in the proximal colon. The distal colon proved to be aganglionic. The delayed roentgenogram established the diagnosis.

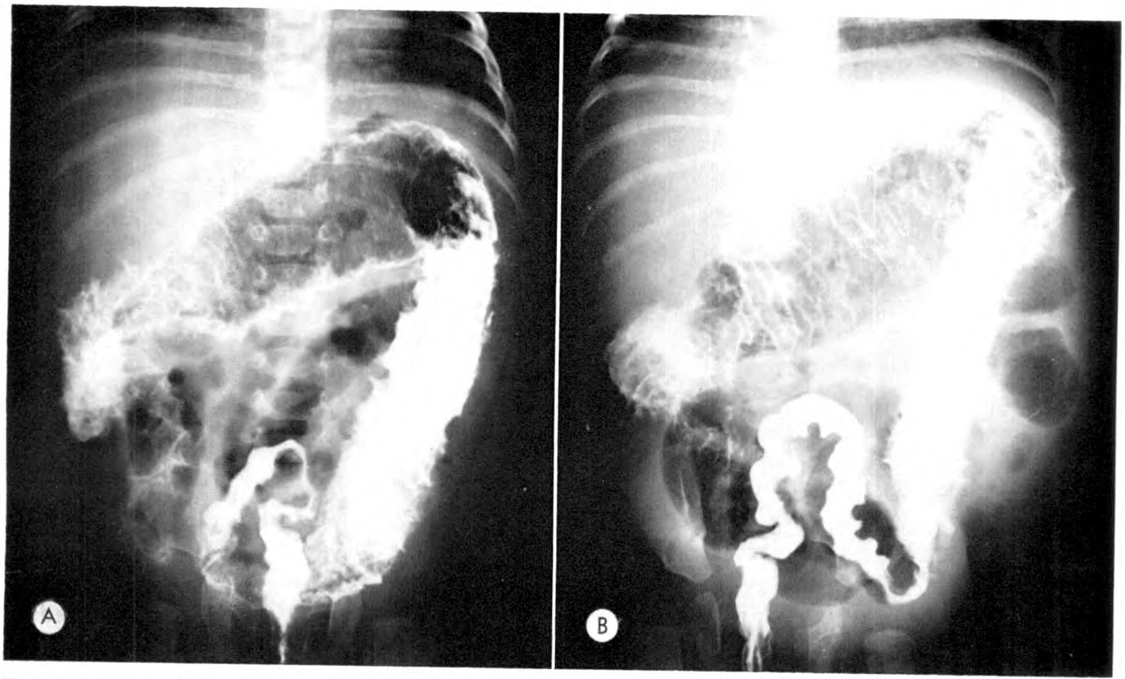

FIG. 11. A pair of 8 week old identical male twins. Each twin had diarrhea during the first 3 weeks of life which gradually changed to constipation. They both developed generalized edema at 6 weeks and were referred to The Children's Hospital of Philadelphia as "atypical" nephrotics. Each had a normal urinalysis, but each had low serum proteins. Plain roentgenograms of the abdomen of each twin showed a distended bowel with a relatively narrow rectum. (*A*) Anteroposterior roentgenogram of the barium-filled colon of one of the twins shows irregular, bizarre, "saw-tooth" contractions of the rectum and sigmoid. A zone of demarcation is noted at the junction of the sigmoid and descending colon. Above this the colon is thick, nodular and edematous, producing a "shaggy" border suggestive of ulcerative colitis. This is the picture of exudative enteropathy. Pathologic examination of the distal segment showed aganglionosis, and, after a primary colostomy and a secondary "pull-through" operation, the baby has had a normal growth and development. (*B*) Anteroposterior roentgenogram of the barium-filled colon of the second twin. The only difference between the two is the position of the sigmoid colon. This baby, after a primary colostomy and a secondary "pull-through" operation, has also grown and developed normally.

each case they were a transient and fleeting phenomenon seen on but one roentgenogram. In infants with Hirschsprung's disease, they are frequently seen and persist throughout the study, chiefly on the after-evacuation roentgenograms (Fig. 8 through 10, inclusive).

5. EXUDATIVE ENTEROPATHY IN THE DILATED PROXIMAL COLON

There is a final diagnostic picture in infantile Hirschsprung's disease: the thickened, nodular, edematous colon seen in the infant with exudative enteropathy secondary to the obstruction caused by the aganglionic segment.[2] These babies present with edema, hypoproteinemia, and usually diarrhea. The appearance superficially mimics ulcerative colitis. The diagnosis can sometimes be made on the plain roentgenograms. These infants usually have a definite zone of transition, but, since they do not have constipation as the presenting symptom, it is important to recognize the possibility of Hirschsprung's disease and perform a colon examination. Our first 2 cases were identical twins referred as suspected atypical nephrotics, "atypical" because each baby's urine was normal (Fig. 11, *A* and *B*).

TECHNIQUE OF EXAMINATION

In spite of all that has been written on the subject, the average baby sent to The Children's Hospital of Philadelphia, already allegedly studied, has had no survey roentgenograms of the abdomen taken, has had either a balloon tip blow up the rectum or a long metal tip inserted all the way to the sigmoid, and views of the full colon only in the anteroposterior projection. The usual diagnosis on admission, therefore, is megacolon, but whether it be functional chronic constipation or true aganglionosis is impossible to say because of the technique of the study. It is not redundant, therefore, to describe our method of study.

In the infant presenting with diarrhea or bowel obstruction, there is no preparation. In the child presenting with constipation, saline cleansing enemas are given, but we do not insist on a perfectly clean colon as for a polyp study.

A preliminary survey roentgenogram or roentgenograms are taken. If the presenting complaint is simply constipation, a single supine view is sufficient, but, if the problem is obstruction, routine anteroposterior supine, anteroposterior erect and left lateral recumbent roentgenograms are taken.

The enema tube is a piece of straight tubing without a balloon, which is inserted 1 inch within the anus.[3] The anal margin is marked by a metal marker. This is not necessary in the lateral views where the pelvic floor is identifiable, but on the oblique roentgenograms it is a worthwhile land mark.

If the history or survey roentgenogram suggests that the possibility of Hirschsprung's disease exists, we perform the enema examination with a water-soluble contrast material in the young infants, and a dilute suspension of barium in normal saline in the older children. If there is an obvious transition zone, we do not fill the colon any more than is required to demonstrate it. This is probably less important using a water-soluble material than when using barium. Barium retention can be remarkably prolonged, and, while not disastrous, impacted barium is notoriously difficult to remove.

The zone of transition is usually best seen in the lateral or oblique roentgenograms so that the baby is turned on his side while the opaque material is filling the rectum. Now it depends on the fluoroscopist to turn the baby into the proper position in order to demonstrate satisfactorily the area of transition. We always conclude the fluoroscopy with an overhead anteroposterior and lateral roentgenogram, both pre and post evacuation. In constipation problems, there is no need to unfold the splenic and hepatic flexures as one does when looking for marginal defects in the adult. The post-evacuation roentgenograms tend to exaggerate all of the pathognomonic roentgen signs we have already discussed. The lateral roentgenograms are imperative in order to identify clearly the rectum and anus. The anteroposterior roentgenograms will often hide a short aganglionic segment because of the ballooning of the proximal bowel overlying the narrowed segment.

Unless a clear-cut diagnosis of Hirschsprung's disease has been reached on the initial study, a 24 hour roentgenogram is taken if barium is used. This is done even if the study appears normal because it is a roentgenogram easy to obtain and, at times, contains almost the only clue. If water-soluble material is used, the 24 hour roentgenogram is of no value but, if the history is highly suggestive and the study in any way equivocal, the examination is repeated, using barium.

This method of study and the pathognomonic signs described will almost always establish a diagnosis, and with proper management will prevent the fulminating complications and mortality that sometimes occur with Hirschsprung's disease.

SUMMARY

During the first few months of life, Hirschsprung's disease is a potentially lethal congenital anomaly. Seldom is constipation the presenting symptom at this age. A significant number of babies presents with the picture of neonatal bowel obstruction, fulminating gastroenteritis, or chronic diarrhea with failure to thrive, the latter

with protein-losing enteropathy as the extreme.

The pathognomonic roentgen signs in infancy are: (1) a zone of transition (if present); (2) irregular, bizarre contractions of aganglionic segment; (3) barium retention following a barium enema study; (4) parallel transverse folds in the dilated proximal colon; and (5) exudative enteropathy in the dilated proximal colon.

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AGANGLIONOSIS OF THE COLON AND TERMINAL ILEUM

LONG TERM SURVIVAL

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COLONIC and terminal ileal aganglionosis is a relatively rare disease and has previously been recognized only in infancy. The prognosis is grave with a mortality approaching 80 per cent, even after early diagnosis and surgical therapy.

The purpose of the author is to report a patient with colonic and terminal ileal aganglionosis who survived with only symptomatic therapy until a diagnosis was made at 13 years of age.

REPORT OF A CASE

This white girl, born on November 19, 1950, was first seen at the University of Arkansas Medical Center on September 29, 1956. History revealed a normal prenatal course and birth. In the second week of life, no bowel movements were noted for 3 days. Suppositories and laxatives were required and were subsequently used through infancy. Only one episode of severe diarrhea was reported; it followed vigorous measures to relieve a particularly prolonged episode of constipation. A physician was consulted at approximately 1 year of age. Roentgenograms were obtained and reported as "normal." Toilet training was limited to attempts to establish a regular pattern but this was unsuccessful. The mother stated that the patient never had the "urge" to have a bowel movement. Fecal soiling was not a problem.

She was seen when 4 years of age at another hospital with a history of stubborn constipation and progressive distention for at least 1 week. Physical examination revealed a large abdomen with palpable fecal masses. A barium enema study was attempted but flow beyond the sigmoid colon was not possible. A volvulus was suspected. Laparotomy showed the entire colon to be dilated from the peritoneal reflection to the cecum. A large fecalith was impacted in the lower sigmoid portion of the colon. This was broken up and the large bowel was deflated from below. Colonic biopsies were not done. A repeat barium enema study was thought to be normal (Fig. 1). The patient did reasonably well for the next 2 years but required frequent enemas and laxatives every 2 to 3 days.

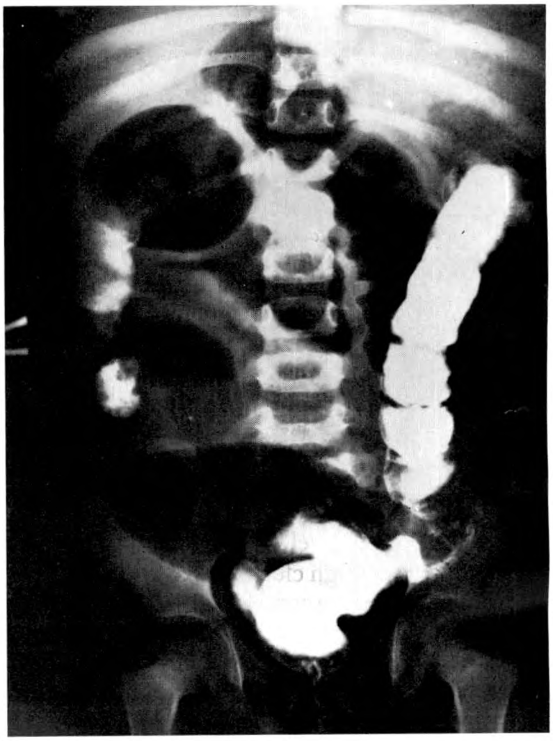

FIG. 1. Postevacuation roentgenogram of barium enema study at the age of 4 years after removal of fecal impaction. Note the relatively normal size of the colon with distended loops of small bowel.

Three siblings were described as normal. There was no history of constipation in any member of the family.

When seen at the University of Arkansas Medical Center, she was a well developed child with a distended abdomen and palpable fecal masses. A barium enema examination was terminated at the splenic flexure because of pain (Fig. 2). Functional megacolon was diagnosed. She was treated with diet, laxatives and enemas as required and did reasonably well for the next 18 months. During the next 6 years she was followed by her local physician.

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In July, 1964 she was again referred to the University of Arkansas Medical Center because of bloating, abdominal cramps, severe constipation and failure to gain weight despite an adequate dietary intake. Constipation alternating with watery stools and nocturnal fecal incontinence had been present for several months.

Physical examination on re-admission revealed a poorly developed child who appeared chronically ill. The abdomen was distended but soft and nontender. Beginning breast development and pubic hair were present. The admitting diagnosis was chronic constipation secondary to functional megacolon.

Laboratory studies were within normal limits. Thyroid function studies were done because of mild retardation of skeletal maturation but were within normal limits.

Plain roentgenograms of the abdomen were thought to show multiple distended loops of small and large bowel with a large amount of feces. After thorough cleansing, a barium enema was done. The colon was filled to a point in the right upper quadrant. Because of complaints by the patient of pain, further filling was not attempted. Several loops of bowel distended with gas and containing what appeared to be haustrations were apparent, separate from the barium column (Fig. 3, *A* and *B*). Because of these findings only partial filling of the colon was presumed to have occurred. A delayed roentgenogram showed satisfactory evacuation (Fig. 3*C*). An excretory urogram was considered normal (Fig. 4).

Although no transition point was recognized, a low aganglionic segment was thought possible because of the patient's history. Rectal biopsy was done on August 6, 1964. Microscopic examination revealed no ganglion cells.

Exploratory laparotomy was performed. The distal portion of the colon at the level of the rectosigmoid was found to be mildly dilated. The remaining portion of the large bowel appeared narrowed with thickening of the walls. The cecum lay in the right upper quadrant with shortening of the entire colon. The distal 25 cm. of ileum was narrowed and thickened. The remainder of the ileum was markedly dilated with the loops larger than the usual colonic size. Biopsies were obtained in the sigmoid, transverse and cecal portions of the colon and in the narrowed portion of the ileum (Fig. 5, *A* and *B*). None showed ganglion cells. A biopsy obtained from the dilated segment of ileum demonstrated ganglion cells (Fig. 5*C*). A tube ileostomy and an ileosigmoid side-to-side anastomosis were performed. The ileum and colon were otherwise left intact.

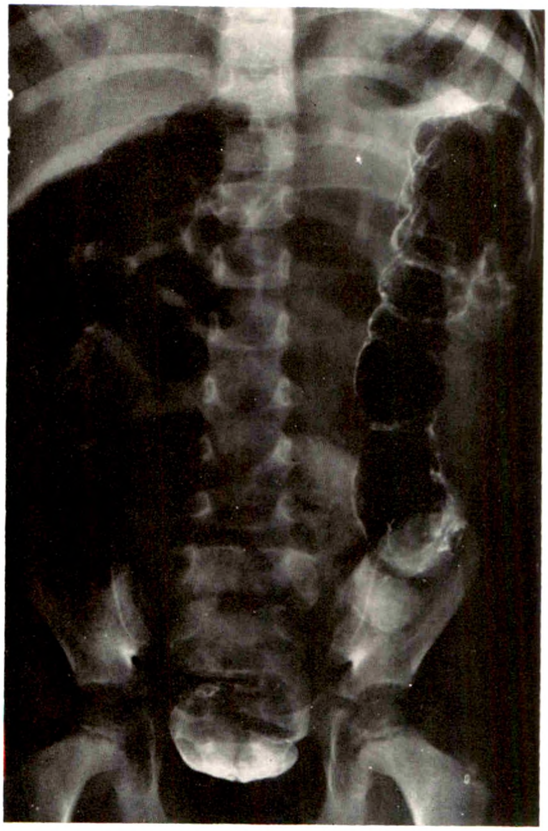

Fig. 2. Postevacuation roentgenogram of barium enema study at the age of 5 years. Again the colon is not dilated but distended loops of small bowel are present.

The postoperative course was benign with the tube ileostomy closed on the 14th postoperative day. On discharge, the patient was having two loose stools per day and gaining weight. On further clinic visits she has continued to do well. On October 23, 1964, she had gained 7 pounds. The abdomen was not distended and bowel movements averaged 2 to 3 per day.

DISCUSSION

Edelman *et al.*[3] in 1960 collected 26 previously reported cases of colonic and terminal ileal aganglionosis and added a 27th of their own. Of the cases collected by them in which the age of the patient was given, the oldest was 3 weeks old[2,5] at the time of diagnosis. Berdon *et al.*[1] subsequently reported 6 cases, 1 of which survived 5 weeks before diagnosis. The latter authors state that no long segment cases of Hirschsprung's disease have been seen beyond early child-

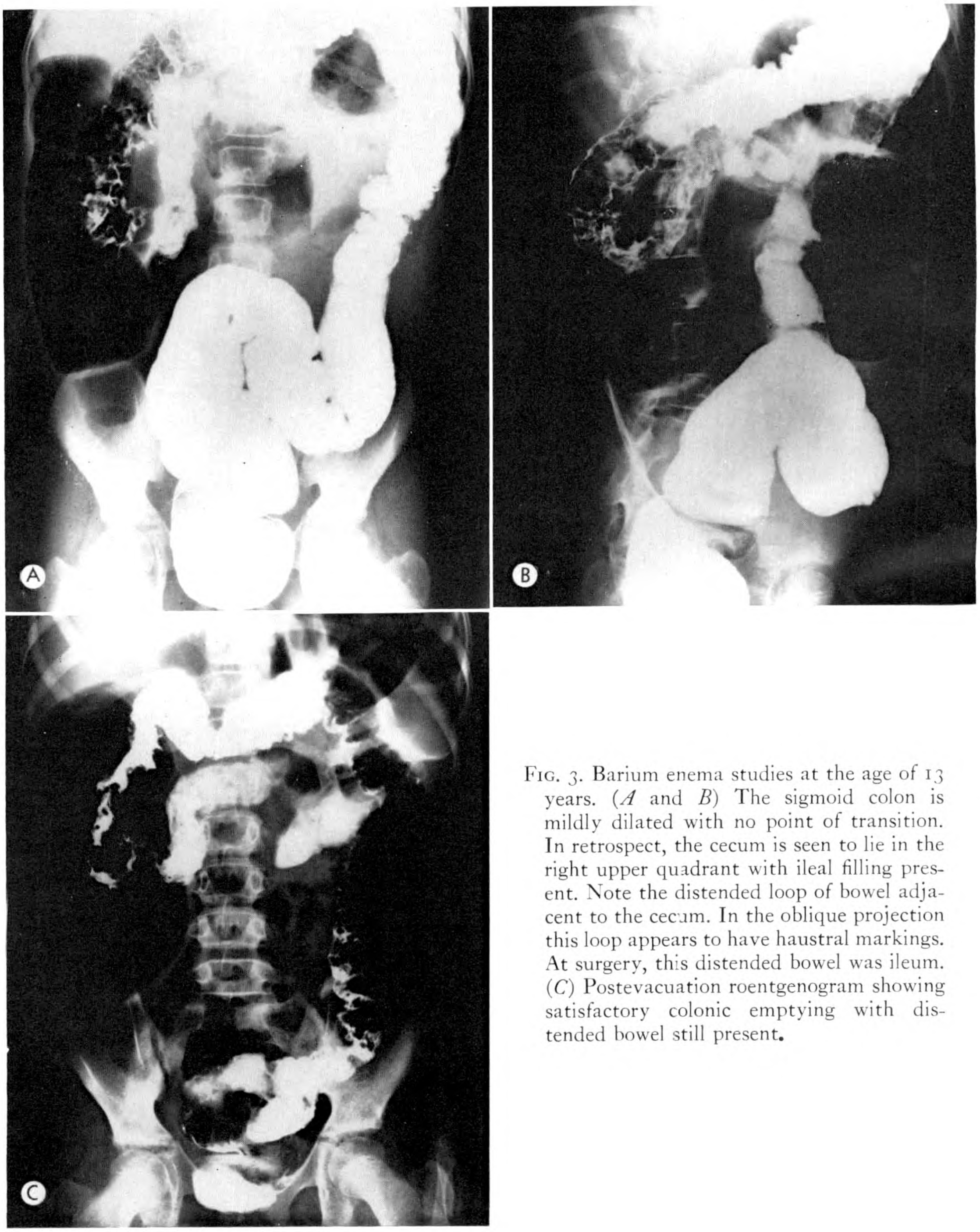

Fig. 3. Barium enema studies at the age of 13 years. (*A* and *B*) The sigmoid colon is mildly dilated with no point of transition. In retrospect, the cecum is seen to lie in the right upper quadrant with ileal filling present. Note the distended loop of bowel adjacent to the cecum. In the oblique projection this loop appears to have haustral markings. At surgery, this distended bowel was ileum. (*C*) Postevacuation roentgenogram showing satisfactory colonic emptying with distended bowel still present.

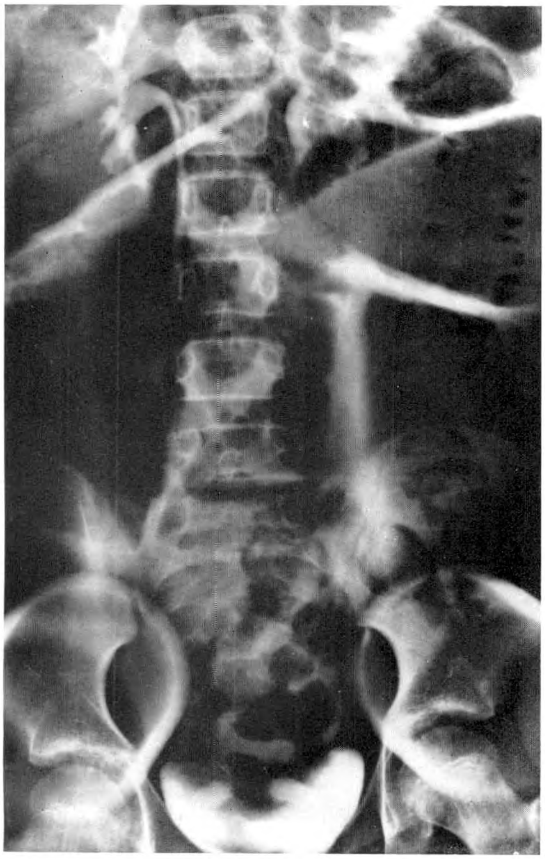

Fig. 4. The excretory urogram appears normal with no evidence of upper urinary tract dilatation.

hood. All previous case reports have emphasized the lethal nature of the disease with enterocolitis often a fatal complication.

Berdon *et al.*[1] described the clinical presentation in these patients as one of intermittent, rather than progressive, obstruction and with bile-tinged emesis. In some patients, distention is not marked and weight gain occurs. However, even with early diagnosis and surgery, the prognosis is grave.

The patient reported in this article has a characteristic history, that of chronic constipation beginning at birth. As often occurs in Hirschsprung's disease, an exploratory laparotomy for obstruction was performed; in this instance at the age of 4. The fecal impaction was considered sufficient cause

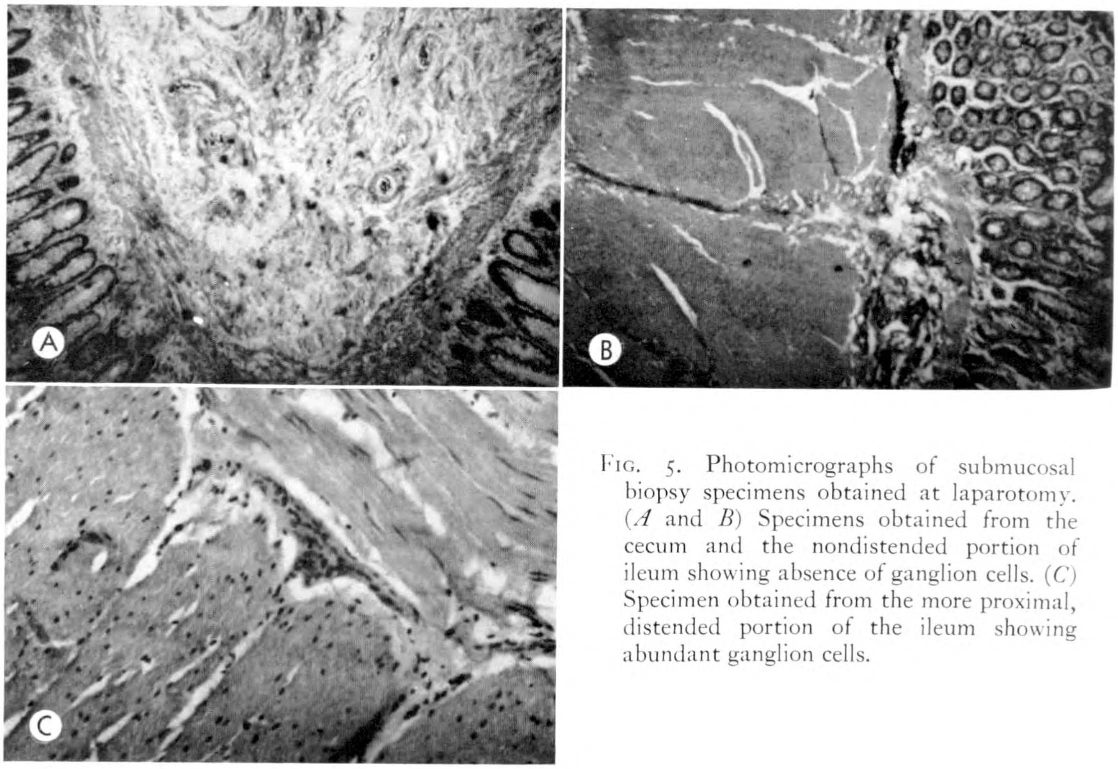

Fig. 5. Photomicrographs of submucosal biopsy specimens obtained at laparotomy. (*A* and *B*) Specimens obtained from the cecum and the nondistended portion of ileum showing absence of ganglion cells. (*C*) Specimen obtained from the more proximal, distended portion of the ileum showing abundant ganglion cells.

for these symptoms and no further diagnostic procedures were performed. She is unique, however, in that she developed no episodes of enterocolitis and managed to survive beyond early childhood. Even more surprising is the relatively benign further course of her disease. Although constipated, she developed at a normal rate, attended school and, in general, led a basically normal life. Her symptoms appear to have become more severe prior to the last hospitalization when, with absence of weight gain and nocturnal fecal incontinence, her local physician was prompted to seek consultation. Fecal incontinence is an unusual finding in Hirschsprung's disease. In this patient the incontinence might be related to the increased use of enemas and laxatives, but this is only conjecture.

In the patients described by Berdon *et al.*,[1] shortening of the colon was a consistent finding at the time of barium enema study. In retrospect, the cecum in this patient was seen to lie in the right upper quadrant and the over-all effect was one of shortening. The more distal portions of the colon were mildly dilated, presumably secondary to the frequent enemas. This shortening was not appreciated initially because the markedly gas-filled ileum simulated loops of colon. So marked is this ileal distention that haustral markings seem present. These same findings were present to a lesser degree in the examinations at the ages of 4 and 6 years.

The question arises as to why this patient survived. Hiatt[4] showed that the aganglionic segment in Hirschsprung's disease is able to contract as a mass action but unable to convey a peristaltic wave. This inefficient mass action may have been sufficient to evacuate this patient's colon with the aid of enemas and laxatives. Further studies as to peristaltic activity in patients with long-segment aganglionosis are indicated.

SUMMARY

1. A patient is reported in whom the diagnosis of colonic and terminal ileal aganglionosis was made at 13 years of age. This long-segment form of Hirschsprung's disease has previously been described only in infancy and has been associated with a grave prognosis, even in case of early diagnosis and surgical therapy.

2. The roentgen finding of a short colon, described in infants with aganglionosis of the entire colon, was also present in this case.

3. The possibility of Hirschsprung's disease should be considered in all patients with constipation beginning in infancy. If shortening of the entire colon is demonstrated, colonic and terminal ileal aganglionosis should be suspected. A rectal biopsy is the definitive procedure.

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ROENTGENOGRAPHY OF THE PRE-ADOLESCENT BREAST*

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BECAUSE of widespread fear and concern on the part of the general public in matters pertaining to the female breast, it is only natural for this anxiety to be accentuated when the patient with the breast problem is a child. An attempt to familiarize the radiologist with the roentgen appearance of the young breast would seem to be in order since he can play a major role in allaying the fears of the apprehensive parents and referring physician. The radiologist can be especially helpful in this problem since we have found that the female breast may begin to develop at a much earlier age than is commonly supposed.

Our series of mammograms in children is necessarily small since relatively few children are referred for roentgenographic examination. For the purposes of this paper, we have collected only those cases from early childhood (exclusive of infancy) to the age of 10 years, because after 10 years the children may properly be considered to be entering adolescence and rarely present any difficulty in clinical diagnosis of breast enlargements and other complaints. The number of cases thus found within the age limits of early childhood and adolescence totals only 12, but, in spite of the small number, their roentgen studies are quite instructive and have shown that the normal breast may begin to develop as early as the age of 6 years.

If roentgenographic examination permits recognition of normal breast tissue at such an early age and thus makes it possible to avoid needless removal of breast tissue for biopsy, it is obvious that a great service has been rendered the patient who might otherwise grow up with one absent or partially undeveloped breast and with the inevitable, attendant psychic difficulties. Of course, at the youthful age of 6 years, abnormal causes of breast enlargement such as feminizing tumors, must be ruled out, but even in such a case it is helpful to be able to prove that a lump in the breast, especially if unilateral, is due merely to hypertrophic mammary tissue.

At birth, the breasts of both sexes consist of branched, dilated ducts containing secretions derived from the ductal epithelium. About 60 per cent of infants exhibit enlargement of the breasts, but up to the age of 6 months this should not be considered pathologic.[1,3] In rare cases the hypertrophy may persist beyond infancy or may regress to return again. Between the age of 6 months and puberty, the ducts lengthen and divide very slowly and the breast may be considered to be in a "resting" stage. Before puberty there is probably no significant difference between the male and female breast. During adolescence and prior to ovulation, the breast consists only of ducts without lobules. Later the ducts branch along their course from the nipple to the pectoral fascia with considerable lack of uniformity of development in different portions of the breast.[6]

In the age group we are concerned with in this paper, childhood to pre-adolescence, the breast contains only small ducts scattered throughout a fibrous stroma.[4] Precocious puberty may perhaps be thought of as occurring before the ages of 8–9 years, and, although feminizing tumors of the ovary, lutein cyst, adrenal cortical tumors and lesions of the 3rd ventricle should be excluded, in most cases no underlying organic cause can be found.[5]

In spite of their limited number, the illustrations shown (Fig. 1 through 7) afford a rather complete survey of the various con-

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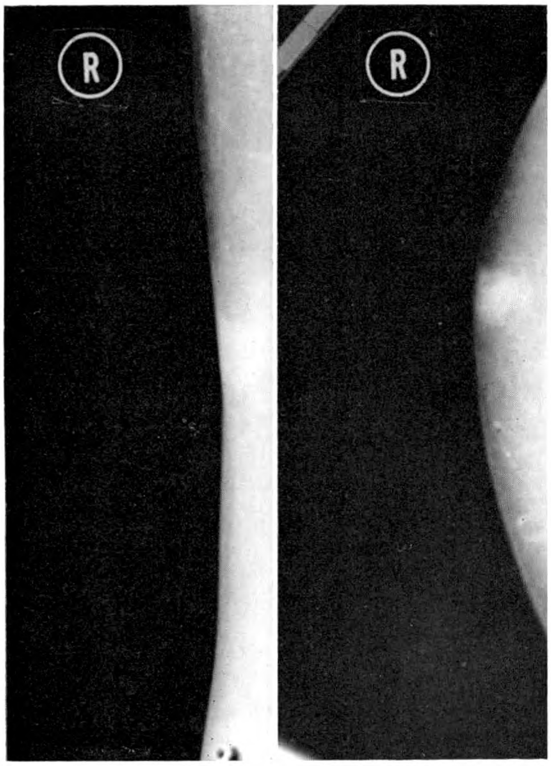

Fig. 1. (C-7110). Right lateral and cephalocaudad roentgenograms in a 9 year old girl showing the earliest duct proliferation beneath the nipple surrounded by subcutaneous fat.

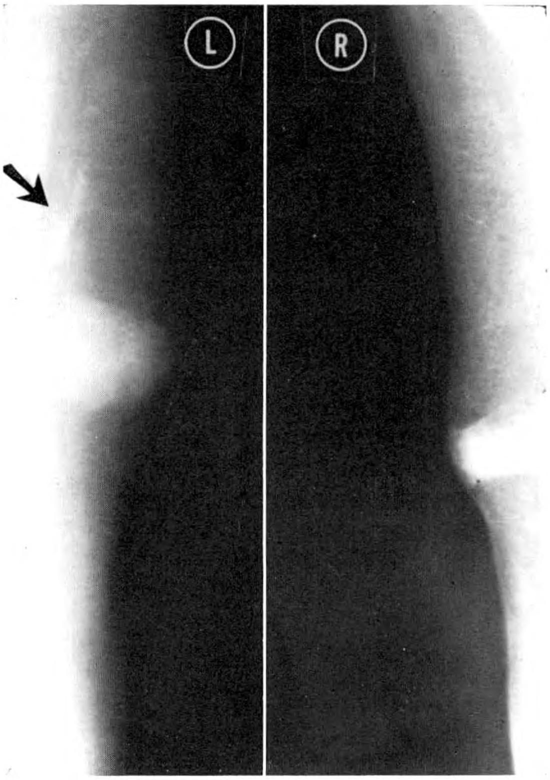

Fig. 2. (C-2840). Left and right lateral roentgenograms in a 10 year old girl showing beginning spread of ducts into the deep prepectoral portion of the breast (arrow).

figurations seen at representative stages in the development of the normal female breast. One notes a striking parallel to the picture seen in gynecomastia in the male which can perhaps be thought of as an early stage of breast development.[2] As in the male, the roentgen picture of the growing female breast varies from a nondendritic, well circumscribed area of density beneath the nipple to a markedly branching pattern of root-like prolongations into the general breast area. The unequal development of one breast as compared with the other should be constantly kept in mind if only

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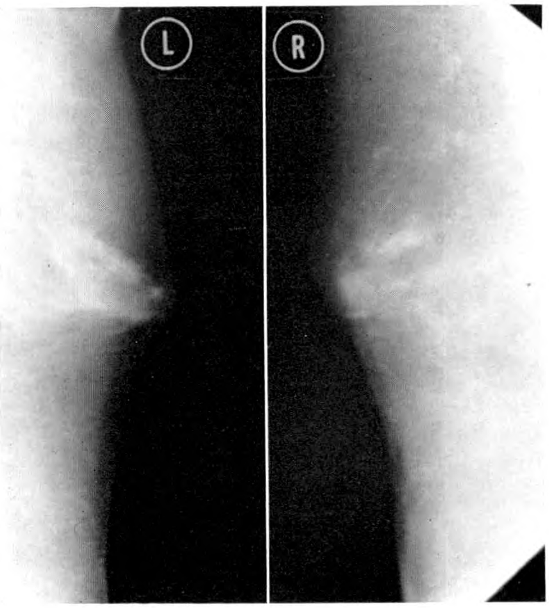

Fig. 3. (C-1609). Left and right lateral roentgenograms in a 10 year old girl demonstrating dendritic type of duct and matrix proliferation with slightly more widespread penetration of deeper tissues than in Figure 2. Note root-like prolongations posteriorly.

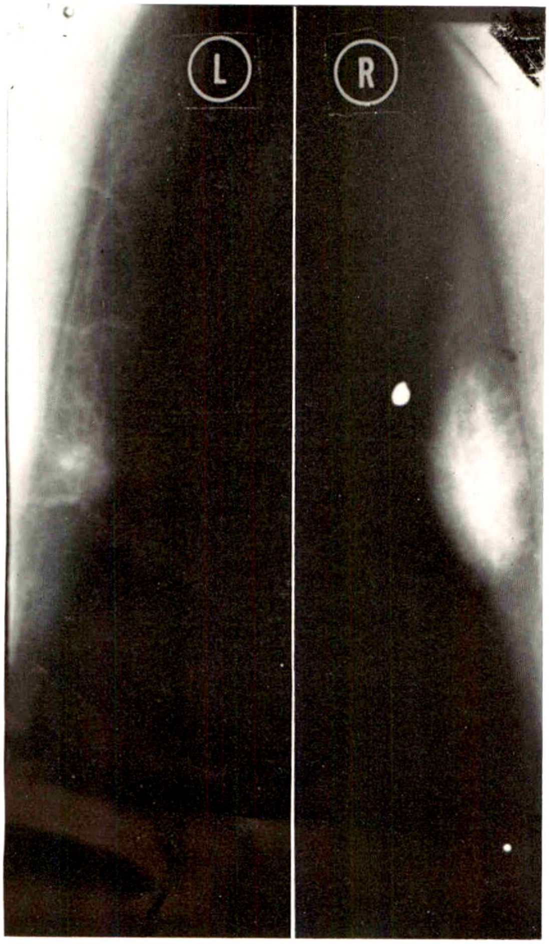

Fig. 4. (C-3433). Left and right lateral roentgenograms in a 9 year old girl showing marked roentgenographic discrepancy in development of right and left breasts. Moderately dendritic variety. This child presented with a painful, 3 cm. lump of 5 months' duration in the right breast. The roentgenograms reveal nothing suggestive of malignancy and reinforce our clinical decision merely to observe the patient. In this way there is further support for nonintervention and possibly avoidance of unnecessary deformity in later life.

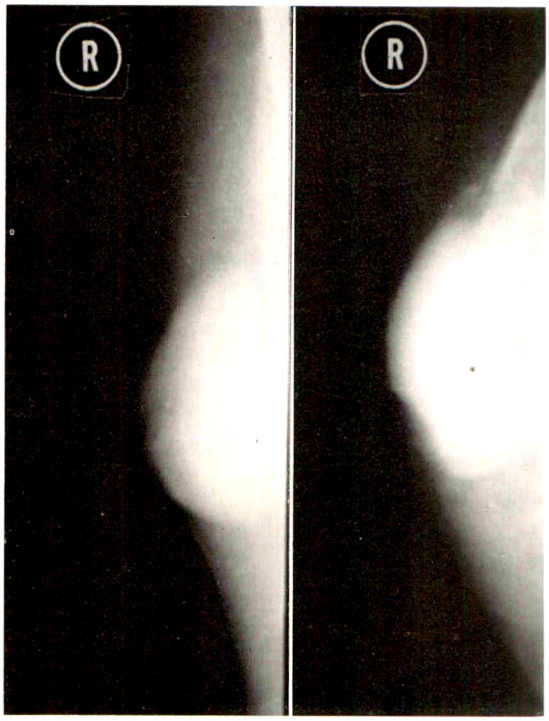

Fig. 5. (C-9354). Right lateral and cephalocaudad roentgenograms in a 16 month old child showing marked breast hypertrophy with no known organic abnormality on 10 month follow-up—a probable case of idiopathic hypertrophy. Note essentially nondendritic, well-circumscribed configuration.

to avoid undue concern about a mistaken impression of a tumor developing in a given breast when the opposite breast clinically appears completely flat and undeveloped. In our experience, the unsuspected breast will invariably exhibit some degree of duct development on roentgenograms. This, together with the rather characteristic roentgen picture and the extreme rarity of neoplastic disease in children's breasts, will almost always obviate the need for biopsy in this age group. Again it must be emphasized that a prepuberal breast, especially female, should be biopsied only with the greatest reluctance. Familiarity with the roentgenographic appearance of the developing breast provides us with effective support for rational conservatism.

SUMMARY

A series of roentgenograms are presented, along with a discussion, showing the typical roentgenographic patterns seen in the developing female breast from childhood to pre-adolescence.

Department of Radiology
Albert Einstein Medical Center
Northern Division
Philadelphia, Pennsylvania

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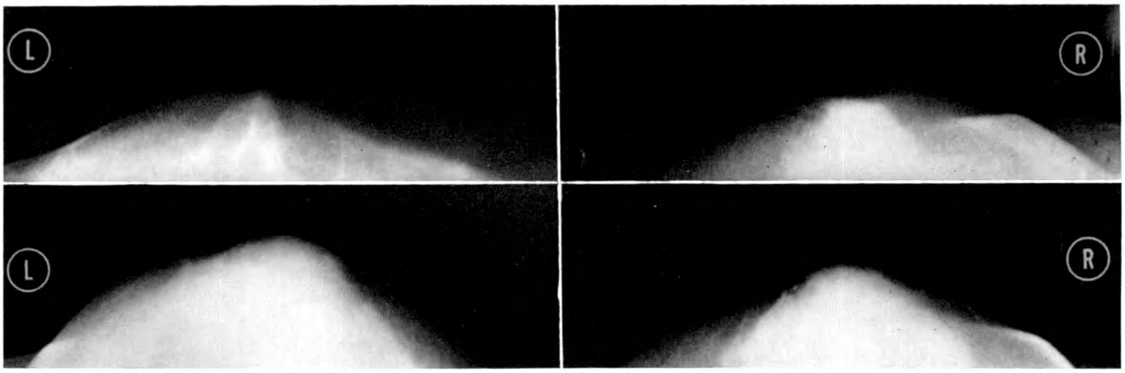

FIG. 6. (C-4980). Seven year old patient. *Top:* Left and right cephalocaudad roentgenograms showing right breast moderately more developed than left—a quite common situation. *Bottom:* Same patient 15 months later. The left breast has now outstripped the right breast in development.

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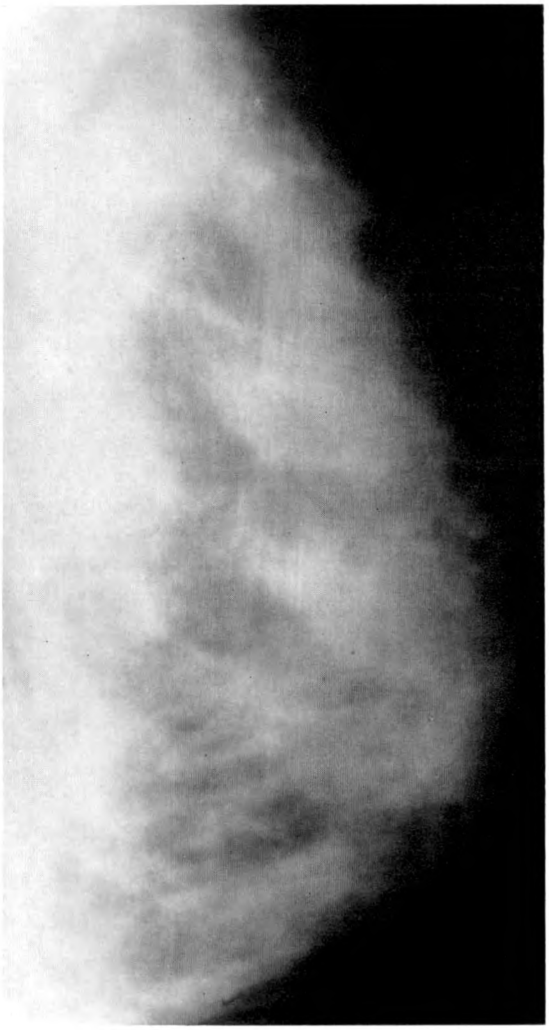

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FIG. 7. (C-7019). Left lateral roentgenogram in a 12 year old girl illustrating substantially an adult stage of development. The trabeculae have spread throughout the breast.

VOL. 95, NO. 1

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

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Sixty-sixth Annual Meeting: Washington Hilton Hotel, Washington, D. C., Sept. 28-Oct. 1, 1965.

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Representative on the Board of Chancellors of the American College of Radiology: Charles G. Stetson.

Forty-eighth Annual Meeting—Golden Anniversary of the American Radium Society: Camelback Inn, Phoenix, Ariz., April 13–16, 1966.

EDITORIAL

PEDIATRIC RADIOLOGY

THIS issue of the JOURNAL contains 32 articles on pediatric radiology. It is perhaps appropriate to ask whether there is any recognizable trend in the specialty of pediatric radiology as reflected by these numerous and varied scientific publications and why an increasing number of radiologists appear to be devoting their time to the sub-specialty of pediatric radiology.

As has been mentioned by a previous editorialist[1] in these pages, one has only to read the splendid history of pediatric radiology on this continent up to 1956 by Dr. John Caffey[2] to appreciate how rapidly the specialty has progressed since the early days of radiology and how many fields of interest are open to the practitioner of this discipline. All through the years of development of pediatric radiology there has been a proper and continuing interest in normal growth and in normal variations. Indeed, one sometimes gets the impression, that the most valuable part the pediatric radiologist plays in daily practice is to prevent over-diagnosis caused by normal findings and normal variations not familiar to those with less experience in the field. The interest, importance, and challenge of recognizing what is not abnormal in infants and children are bound to continue in the foreseeable future, and at least 3 of the articles this month contain further contributions in this area.

Although skeletal trauma in infants and children has been extensively studied and documented by radiologists and surgeons, the problems of closed chest and abdominal trauma are perhaps not as fully reported and documented in the literature. The incidence, however, of severe and even fatal chest and abdominal trauma due to "closed" injuries without fracture of bones is likely to be a good deal higher in children than in adults because the bones of the infant and child are more elastic, while the internal organs are at least equally susceptible to contusion and laceration in comparison with adult structures. It is, therefore, appropriate that 2 of the articles this month are devoted to the subject of closed trauma.

Diagnosis in the newborn infant is far more frequent and more successful today than ever before. This is due in no small measure to the efforts of the pediatric radiologist, working in cooperation with the specialists in another, even newer field—neonatology. Of the problems threatening the life of a newborn child and in the diagnosis of which the pediatric radiologist can legitimately be interested, respiratory disease, congenital heart disease, and obstruction of the gut perhaps are the commonest, in about that order of frequency. They all seem to be getting commoner, but this is at least partially due, in all likelihood, to higher and higher standards of care and of diagnostic facilities and skill. Hirschsprung's disease, in particular, is highly lethal if not recognized, but is now susceptible to very satisfactory surgical management for the most part, providing the diagnosis is made sufficiently early—and sufficiently early has now come to mean within a few days of birth. The present group of papers contains several contributions in this area of neonatal diagnosis and management.

Anyone who asks a pediatric radiologist to present an essay or to write an editorial is bound to expose himself and the medical public to a modicum of moralizing and sermonizing on the subject of radiographic technique. The present writer cannot, any more than any other in his field, resist the temptation to "point with pride" to the improved facilities and methods for radiography of infants and children and "view with alarm" the lamentable state of the art in all but pediatric X-ray Departments, and the deplorable films received from the "other hospital." Indeed, the temptation to deliver a screed, or at least a disquisition, is almost irresistible. However, we shall content ourselves with noting that the papers presented in this issue contain two contributions having to do with radiographic techniques, one of which—by Doctor O'Hara and his colleagues—holds out considerable hope for solving the problem of exposing chest films in inspiration.

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[1] SINGLETON, EDWARD B. Society For Pedriatic Radiology. Editorial. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1964, *91*, 706–707.

[2] CAFFEY, JOHN. The first sixty years of pediatric roentgenology in the United States—1896 to 1956. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1956, *76*, 437–454.

Since the earliest studies by Pancoast in 1906 on skeletal changes in achondroplasia and cretinism, radiologists, and, particularly, pediatric radiologists, have been struggling with the problem of classifying generalized malformations of bone and cartilage. This year is no exception; several papers appear in this issue on generalized skeletal malformations, as the effort continues to classify and understand abnormalities which at times seem to be unclassifiable and inexplicable.

On Monday, the 27th of September, 1965, the Society for Pediatric Radiology will hold its Annual Meeting at the Washington-Hilton Hotel, Washington, D.C., and the Scientific Program contains some of the papers published in these pages, and a number of others unpublished; indeed, the emphasis in the Society for Pediatric Radiology has tended to be on new and unpublished material, presented as much for discussion and exchange of information as for definitive recording. This meeting has, because of its lively and informal nature, tended to include as much a series of dialogues as of formal papers.

Can one recognize a trend in pediatric radiology from all this material? It seems to the present writer that what is appreciable from the material being published herein is the great diversity of interests and the challenge in what started out as a small sub-specialty. The practitioner of pediatric radiology can feel today more than ever that a large number of scientific avenues of investigation are open to him, and that he can continue down any one of these fascinating paths of research. Or, he can remain in contact, within this one seemingly small area, with a tremendously stimulating group of surgical and medical specialties so that he, in some respects, has the best of both worlds—he is in a subspecialty within the general field of radiology, yet he is a general consultant to a number of other specialists, all of whom have in common an interest in the normal and abnormal phenomena in infancy and childhood.

J. S. DUNBAR, M.D.
President
Society for Pediatric Radiology

Director, Department of Radiology
The Montreal Children's Hospital
Montreal 26, Quebec, Canada

NEWS ITEMS

THE AMERICAN BOARD OF RADIOLOGY

Beginning with the examination in Dallas, Texas, December, 1965, all candidates for certification in Diagnostic Roentgenology will be examined in the Diagnostic aspects of Nuclear Medicine and should be so prepared.

H. Dabney Kerr, M.D.
Secretary

POSTGRADUATE COURSE IN RADIOLOGY OF BONE AND JOINT DISEASES

The Department of Radiology of Emory University School of Medicine will conduct a postgraduate course, "Radiology of Bone and Joint Diseases," on November 5–6, 1965. This course will be held at Grady Memorial Hospital, Atlanta, Georgia.

The guest faculty will be Dr. John Caffey, Children's Hospital of Pittsburgh; Dr. Harold G. Jacobson, Montefiore Hospital, New York; Dr. Lent C. Johnson, Armed Forces Institute of Pathology; Dr. David G. Pugh, Mayo Clinic; and Dr. Howard L. Steinbach, University of California.

For further information, please write to H. S. Weens, M.D., Department of Radiology, Emory University School of Medicine, Atlanta, Georgia 30322.

POSTGRADUATE COURSE IN ADVANCES IN RADIOACTIVE SCANNING

A postgraduate course in "Advances of Radioactive Scanning" will be held at the Penn Sheraton Hotel, October 21–22, 1965, under the directorship of Yen Wang, M.D., D.Sc. (Med.), Associate Professor of Radiology at the Presbyterian-University Hospital, University of Pittsburgh.

The course will include discussion by a guest faculty of outstanding repute on the current methods of dynamic scanning and their clinical application. There will be ample time for informal discussion and consultation. Special emphasis will be placed on rapid scintillation scanning, the use of the scintillation camera and image scanning.

Further information may be obtained from Dr. Campbell Moses, Director of Postgraduate Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15213.

COURSE IN SPECIAL RADIATION PROCEDURES IN THE TREATMENT OF CANCER

The Long Island Jewish Hospital, Queens Hospital Center Affiliation, Division of Radiation Medicine presents a course in Special Radiation Procedures in the Treatment of Cancer, October 18–22, 1965.

There will also be an "Operative Radium Therapy Day" on October 20, 1965, in the operating rooms.

The faculty will consist of members of the Division of Radiation Medicine as well as invited guest lecturers.

The enrollment is limited.

For further information please write to Leonard B. Goldman, M.D., The Long Island Jewish Hospital, Queens Hospital Center Affiliation, 82-68 164th Street, Jamaica, New York, 11432.

CLINICAL CONFERENCE ON CANCER OF THE GASTROINTESTINAL TRACT

"Cancer of the Gastrointestinal Tract" will be the subject of the Tenth Annual Clinical Conference to be held at The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas, on November 5 and 6, 1965. Outstanding scientists and physicians from institutions throughout the United States will join staff members from The University of Texas M. D. Anderson Hospital and Tumor Institute in presenting the most current information on diagnostic procedures and treatment for tumors of the liver and pancreas, cancer of the stomach and small bowel, and carcinoma of the colon and rectum.

Partial support for this year's clinical conference has been contributed by the American Cancer Society, Texas Division; a Community Cancer Demonstration Project Grant from the Cancer Control Program, United States Public Health Service; and the Doubleday Fund.

TEACHING, TRAINING AND RESEARCH PROGRAM IN X-RAY SCIENCES

The Public Health Service, U. S. Department of Health, Education, and Welfare, signed a contract with Oregon State University for the development of teaching and training programs in x-ray sciences. This program will be under the direction of Dr. E. Dale Trout, Professor of Radiological Physics at Oregon State University.

"Programs developed at Oregon State University will be tested and then presented to the Division in such form that they may be used as models for similar programs at other institutions," said Dr. Donald R. Chadwick, Chief of the Division of Radiological Health.

The University also will develop a unit to carry out research, evaluation and development projects in X-ray science and engineering, such as evaluation of instruments used in X-ray measurement, development of a methodology for the evaluation of X-ray protective devices and materials, and methodology and instrumentation for the measurement of X-radiation.

SPACE RADIATION BIOLOGY

A workshop conference on space radiation biology will be held September 7–10, 1965, at the University of California, Berkeley. Sponsors are the National Aeronautics and Space Agency, the University's Donner Laboratory, the Lawrence Radiation Laboratory, and University of California Extension.

The meeting is designed to bring together scientists from several nations who are working in areas related to the biophysics of space radiations and the biologic effects of densely ionizing radiations. Its objective is to discuss recent developments and establish guidelines for future research. Attendance is by invitation.

Scheduled session topics are: Radiologic physics; heavy ion effects on mammalian systems; space radiation hazards to man; molecular effects; evaluation of the combined effects of radiation and other stresses in space flight; and cellular effects.

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BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

CONGENITAL HEART DISEASE: CORRELATION OF PATHOLOGIC ANATOMY AND ANGIOCARDIOGRAPHY. By Jesse E. Edwards, M.D., Director of Laboratories, The Charles T. Miller Hospital, St. Paul, Minn.; Clinical Professor of Pathology, Medical School and Professor of Pathology, Graduate School, University of Minnesota, Minneapolis, Minn.; Lewis S. Carey, M.D., Director, Cardiovascular Diagnostic Unit, Department of Radiology, St. Joseph's Hospital, St. Paul, Minn.; Clinical Assistant Professor, Department of Radiology, University of Minnesota Medical School Minneapolis, Minn.; Henry N. Neufeld, M.D., Chief, Heart Institute, Tel-Hashomer Government Hospital, Israel; Formerly; Research Associate, The Charles T. Miller Hospital, St. Paul, Minn.; Honorary Fellow, University of Minnesota, Minneapolis, Minn. and Richard G. Lester, M.D., Chairman, Department of Radiology, Medical College of Virginia, Richmond, Va. In Two Volumes. Cloth. Pp. Volume I, pp. 1 to 396; Volume II, pp. 397 to 890, with many illustrations. Price, $45.00 the set. W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1965.

The preparation of a comprehensive reference work encompassing the variety of forms and detailed nature of congenital heart disease represents a tremendous undertaking. The correlation of pathologic anatomy with plain roentgenographic and angiocardiographic findings provides additional challenge for the organization of the material.

Radiologists, pathologists and surgeons, to mention just a few of the many physicians dealing with this diagnostic enigma, will praise the authors' accomplishment and benefit from their labors. These volumes should aid in the integration of ideas formed by diverse groups who, together, strive to correctly diagnose and successfully manage congenital heart disease.

Examination of the credentials of the four co-authors reassures all concerned that the most up-to-date material has been assembled. The authors' own combined experience with the pathologic and radiologic aspects of congenital heart disease is reflected in their numerous contributions to the recent literature.

The organization of the two-volume work centers around the introduction of a classification of congenital heart disease, based upon the roentgenographic appearance of the pulmonary vasculature and the presence or absence of cyanosis. Although primarily designed to aid the front guard physician who initially uncovers the abnormality, this system of classification should be acceptable to all specialists concerned.

Each of the five general categories in the classification is composed of numerous individual and combined defects. The general groups are divided into two volumes and discussed thoroughly.

The basic defect or anomaly is introduced by a Section on general considerations. Following this, come Sections on pathologic anatomy and physiology, clinical findings, roentgenographic demonstrations, angiocardiographic procedures, and other interesting features or helpful diagnostic examinations.

Accompanying the discussion in each section are photographs of pathology specimens, reproductions of plain and special study roentgenograms, and diagrams if more detailed description is felt desirable.

Presentation of the material is systematic and concise, covering each entity in a style that is easily comprehended. Occasional overlap of subject matter is encountered as certain anomalies appear under more than one general classification, depending upon the pathologic physiology involved.

The illustrations of the pathology specimens are superb, as are the reproductions of the roentgenograms. Both occupy a prominent part in the educational opportunity provided by these volumes.

The authors have achieved their goal of providing a comprehensive review of congenital heart disease based on the anatomy and physiology of the abnormality, as reflected in available diagnostic procedures, with great authority and in a singularly skillful manner.

GENE MADDOCK, M.D.

Dorland's Illustrated Medical Dictionary. Twenty-fourth Edition. Paper. Pp. 1724. Price, $13.00, Deluxe Edition $17.00. W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1965.

The American Illustrated Medical Dictionary by W. A. Newman Dorland consisted of 770 pages when first published in 1900. Since that year 23 new editions have appeared. The present 24th Edition consists of 1724 pages and contains more than 130,000 definitions—or 20,000 more than the 23rd Edition which appeared in 1957.

This enormous material has been assembled step by step throughout the years, and, in this new edition, it was scrupulously revised and verified by a distinguished Board of Editorial Consultants, each an authority in his field of special responsibility, aided by the invaluable help of 58 eminent contributors.

Effort has been made to retain of the old what has become standard usage and to embrace of the new what appropriately can be built upon the old. Accordingly, many names, definitions and some illustrations have been deleted, but many more have been added or updated, and many existing illustrations have been redrawn. This dichotomy of purpose resulted in the most extensively changed edition in Dorland's long and illustrious history.

Among the most notable changes are: an especially thorough-going reorganization of the anatomical nomenclature, based on the Nomina Anatomica terminology; a complete updating of the drug names, with definitions of the generic names and listing of the proprietary names referring to the generic names; a revision of all entries in microbiology, hematology, dermatology and dentistry, with the addition of the new Glossary of Prosthodontic Terms; a review of pertinent information in clinical medicine and of all historical information, with inclusion of the names of the winners of Nobel prizes in medicine and physiology; and other important items.

Prominent among the Editorial Consultants was the recently deceased Dr. Otto Glasser, of the Cleveland Clinic Foundation, who for many years contributed information on the ever-expanding Language of Radiology.

The American Journal of Roentgenology, Radium Therapy & Nuclear Medicine, as a result of a practice initiated in 1912, and consistently followed since then, built in the domain of medical radiology a style which has become its characteristic feature. The final authority on the spelling and usage of medical terminology (with a few exceptions) in developing this style was always Dorland's Illustrated Medical Dictionary. It is a distinct pleasure, therefore, to welcome the publication of this latest, the 24th Edition.

T. Leucutia, M.D.

BOOKS RECEIVED

A Textbook of Elementary Radiography for Students and Technicians, By Donald deForest Bauer, M.D., C.M., M.Sc., D.A.B.R., Associate Radiologist, Klamath Valley Hospital and Presbyterian Intercommunity Hospital; Associate Professor of Medical X-Ray Technology, Oregon Technical Institute, Klamath Falls, Oregon; Radiologist at Modoc Medical Center, Alturas and Cedarville, Calif.; with a Foreword by Benjamin Goldberg, M.D., D.A.B.R. Cloth. Pp. 241, with a few figures. Price, $8.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1965.

The Roentgen Diagnosis of Trauma. By Herbert R. Zatzkin, M.D., F.A.C.R., Chairman, Department of Radiology, Meadowbrook Hospital, the Nassau County Public General Hospital, East Meadow, Long Island, N.Y.; Consultant Radiologist, Community Hospital, Glen Cove, N.Y.; Consultant Radiologist, Hempstead General Hospital, Hempstead, N.Y.; Consultant Radiologist to the Office of the Medical Examiner, Nassau County, N.Y. Cloth. Pp. 448, with 591 illustrations. Price, $22.00. Year Book Medical Publishers, Inc., 35 E. Wacker Drive, Chicago, Ill., 1965.

Chemical Protection against Ionizing Radiation. By Zénon M. Bacq, Professor at the University of Liège, Belgium; Member, Académie Royale, Classe des Sciences; Member, Académie Royale de Médecine de Belgique; Foreign Member, Academy of Sciences U.S.S.R. With an Introduction by Shields Warren, M.D. Cloth. Pp. 328, with some illustrations. Price, $14.00. American Lecture Series, No. 599. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1965.

Radioactivity in Man. Second Symposium. Whole Body Counting and Effects of Internal Gamma Ray-Emitting Radioisotopes. A Symposium sponsored by Northwestern University Medical School and the American Medical Association. Edited by George R. Meneely, M.D., General Chairman; and Shirley Motter Linde, Symposium Coordinator. Cloth. Pp. 616, with many illustrations. Price, $24.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1965.

LIVING WITH CEREBRAL PALSY. A Study of School Leavers Suffering from Cerebral Palsy in Eastern Scotland. By T. T. S. Ingram, Stella Jameson, Jane Errington, and R. G. Mitchell. With a Foreword by Professor R. W. B. Ellis. Clinics in Developmental Medicine No. 14. Cloth. Pp. 106, with many illustrations. Price, $3.00. Published by The Spastics Society Medical Education and Information Unit in association with William Heinemann Medical Books Ltd., London, England, 1964.

FRACTURE OF THE SHAFT OF THE TIBIA: 492 CONSECUTIVE CASES IN ADULTS. Importance of Soft Tissue Injury. By Per Edwards. Paper. Pp. 94, with some illustrations. Acta Orthopaedica Scandinavica, Supplementum No. 76. Munksgaard, Copenhagen, 1965.

STABLE CALCIUM ISOTOPES AS TRACERS IN STUDIES OF MINERAL METABOLISM. By G. Duncan McPherson. Paper. Pp. 86, with some illustrations. Acta Orthopaedica Scandinavica, Supplementum No. 78. Munksgaard, Copenhagen, 1965.

INFLUENCE OF POSTMORTAL STORAGE ON TENSILE STRENGTH CHARACTERISTICS AND HISTOLOGY OF RABBIT LIGAMENTS. By A. Viidik, L. Sandqvist, and M. Mägi. Paper. Pp. 38, with some illustrations. Acta Orthopaedica Scandinavica, Supplementum 79. Munksgaard, Copenhagen, 1965.

* * *

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society

Secretary, Dr. C. Allen Good, Mayo Clinic, Rochester, Minn. Annual meeting: Washington Hilton Hotel, Washington, D. C., Sept. 28–Oct. 1, 1965.

American Radium Society

Secretary, Dr. John L. Pool, 444 East 68th Street, New York, N. Y. 10021. Annual meeting: Camelback Inn, Phoenix, Ariz., April 13–16, 1966 (Golden Anniversary).

Radiological Society of North America

Secretary-Treasurer, Dr. Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb. Annual meeting: Palmer House, Chicago, Ill., Nov. 28–Dec. 3, 1965.

American College of Radiology

Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Drake Hotel, Chicago, Ill., Feb. 1–5, 1966.

Section on Radiology, American Medical Association

Secretary, Dr. Clyde A. Stevenson, Sacred Heart Hospital, West 101 Eight Ave., Spokane 4, Wash. Annual meeting: Chicago, Ill., June 26–30, 1966.

American Board of Radiology

Secretary, Dr. H. Dabney Kerr. Correspondence should be directed to Kahler Hotel Building, Rochester, Minn.

The Fall 1965 examination will be held at the Statler Hilton Hotel, Dallas, Texas, December 5–10, inclusive. Beginning with this examination, all candidates for certification in Diagnostic Roentgenology will be examined in the Diagnostic aspects of Nuclear Medicine.

The Spring 1966 examination will be held at the Terrace Hilton Hotel, Cincinnati, Ohio, June 6–10, inclusive. The deadline for filing applications for this examination is December 31, 1965.

The Fall 1966 examination will be held at the Washington Hilton Hotel, Washington, D.C., December 5–9, inclusive. The deadline for filing applications is June 30, 1966.

American Association of Physicists in Medicine

Secretary, Leonard Stanton, Hahnemann Medical College, 230 N. Broad St., Philadelphia, Pa. 19102. Annual meeting to be announced.

American Club of Therapeutic Radiologists

Secretary, Dr. J. A. del Regato, Penrose Cancer Hospital, Colorado Springs, Colo.

Eleventh International Congress of Radiology

Secretary-General, Professor Dr. Med. Arduino Ratti, via Moscova, 44-1, Milan, Italy. Address inquiries to Professor Dr. Med. Luigi Turano, President-Elect, Istituto di Radiologia, Università di Roma, Rome, Italy. Meeting: September 22–28, 1965.

Ninth Inter-American Congress of Radiology

Counselor for the United States, Dr. Philip J. Hodes, Jefferson Medical College Hospital, 11th and Walnut Streets, Philadelphia 7, Pennsylvania.
Meeting: Montevideo, Uruguay, 1967.

Alabama Radiological Society

Secretary, Dr. Walter Brower, Birmingham, Ala. Meets time and place of Alabama State Medical Association.

American Nuclear Society

Treasurer, Raymond Maxson, 86 E. Randolph St., Chicago, Ill. Annual meeting to be announced.

Arizona Radiological Society

Secretary-Treasurer, Dr. George Gentner, 3435 W. Durango, Phoenix, Ariz. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Chapter of American College of Radiology

Secretary-Treasurer, Dr. James R. Morrison, 550 S. University, Little Rock, Ark. 72205.

Arkansas Radiological Society

Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Association of University Radiologists

Secretary-Treasurer, Dr. Morton M. Kligerman, Dept. of Radiology, Yale University Medical School, New Haven, Conn. Annual meeting: University of Arkansas, Little Rock, Ark., May 13–14, 1966.

Atlanta Radiological Society

Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

Bavarian-American Radiologic Society

Secretary, Dr. Roy R. Deffebach, Major, MC, Radiology Service, 5th General Hospital, APO 154, New York, N. Y. Meets quarterly.

Blockley Radiological Society

Secretary, Dr. Bernard J. Ostrum, 2412 North 52nd St., Philadelphia, Pa.

Bluegrass Radiological Society

Secretary-Treasurer, Dr. Arthur Lieber, University of Kentucky, University Hospital, Lexington, Kentucky. Meets quarterly.

Brooklyn Radiological Society

Secretary, Dr. Edward Feely, St. Johns Episcopal Hospital, 480 Herkimer St., Brooklyn, N. Y. Meets first Thursday of each month, October through June.

Buffalo Radiological Society

Secretary. Dr. Richard Munschauer, 130 Hodge Ave., Buffalo, N.Y. 14222. Meets second Monday evening each month, October to May inclusive.

California Radiological Society

Secretary, Dr. L. Henry Garland, Suite 1739, 450 Sutter St., San Francisco, Calif. Meets annually during meeting of California Medical Association.

Catawba Valley Radiological Society

Secretary, Dr. Emmett R. White, P. O. Box 303, Rutherford College, N. C. Meets every Tuesday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C. at 12:00 P.M.

Central New York Radiological Society

Secretary-Treasurer, Dr. Edward W. Carsky, Crouse-Irving Hospital, 820 S. Crouse Ave., Syracuse, N. Y. Meets first Monday each month, October through May.

Central Ohio Radiological Society

Secretary-Treasurer, Dr. Harold W. Long, 81 S. Fifth St., Columbus 15, Ohio. Meets third Thursday in October, and second Thursday in November, January, March and May at Fort Hayes Hotel, Columbus, Ohio.

Central Society of Nuclear Medicine

Secretary, Dr. Robert S. Landauer, Radiation Center Bldg., 1903 West Harrison St., Chicago 12, Ill.

Chicago Roentgen Society

Secretary-Treasurer, Dr. Robert D. Moseley, Jr., Dept. of Radiology, Univ. of Chicago, 950 E. 59th St., Chicago 37, Ill. Meets second Thursday of each month, October to April except December at the Pick-Congress Hotel at 8:00 P.M.

Cleveland Radiological Society

Secretary-Treasurer, Dr. James Christie, 10515 Carnegie Avenue, Cleveland, Ohio. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Colorado Radiological Society
Secretary, Dr. David J. Stephenson, 8300 West 38th Ave., Wheat Ridge, Colo. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. William W. Walthall, Jr., 130 Maple St., Springfield, Mass. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary, Dr. R. E. Collier, 3500 Gaston Ave., Dallas, Tex. Meets monthly, third Monday, at Southwest International Airport at 6:30 p.m.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. Robert L. Willis, Harper Hospital, Detroit 1, Mich. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 p.m.

East Bay Roentgen Society
Secretary, Dr. William G. Faraghan, 450 30th St., Oakland 9, Calif. Meets first Thursday each month at University Club, Oakland, Calif.

East Tennessee Radiological Society
Secretary, Dr. C. H. Kimball, 2200 Harris Circle, Cleveland, Tenn. Meets in January and September.

Eastern Radiological Society
Secretary, Dr. James F. Martin, North Carolina Baptist Hospital, Winston-Salem, N. C.

Florida Radiological Society
Secretary, Dr. Andre S. Capi, 3471 N. Federal Highway, Fort Lauderdale, Fla. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Garth R. Drewry, Tampa General Hospital, Tampa 6, Fla. Meets in January, April, July and October.

Georgia Radiological Society
Secretary, Dr. I. R. Berger, 1010 Prince Ave., Athens, Ga. Meets in spring and fall with Annual State Society Meeting.

Greater Miami Radiological Society
Secretary-Treasurer, Dr. Oliver P. Winslow, Jr., Baptist Hospital of Miami, Inc., 8900 S. W. 88th St., Miami 56, Fla. Meets monthly, third Wednesday at 8:00 p.m. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary-Treasurer, Dr. Mark D. Eagleton, 950 Francis Place, St. Louis, Mo.

Houston Radiological Society
Secretary, Dr. D. A. Van Velzer, Texas Medical Center Library, Jesse H. Jones Library Bldg., Houston 25, Tex. Meets fourth Monday of each month, except June, July, August and December, at the Doctors' Club, 8:00 p.m., Houston, Tex.

Idaho State Radiological Society
Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Society
Secretary, Dr. George A. Miller, Carle Hospital Clinic, Urbana, Ill. Meets in the spring and fall.

Indiana Roentgen Society, Inc.
Secretary, Dr. Richard A. Silver, 1815 N. Capitol Avenue, Indianapolis, Ind. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary, Dr. L. L. Maher, 1419 Woodland Ave., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary-Treasurer, Dr. Robert C. Lawson, 310 Medical Arts Bldg., 10th and Home, Topeka, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter, American College of Radiology
Secretary-Treasurer, Dr. Robert H. Greenlaw, Dept. of Radiology, Univ. of Kentucky Med. Ctr., Lexington, Ky. Meetings will be semiannually.

Kentucky Radiological Society
Secretary-Treasurer, Dr. Joan R. Hale, 402 Heyburn Building, Louisville, Ky. Meets monthly on second Friday at Sheraton Hotel, Louisville, Ky.

Kings County Radiological Society
Secretary, Dr. Stanley Dannenberg, 1917 Bedford Ave., Brooklyn 25, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 p.m.

Knoxville Radiological Society
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Long Island Radiological Society
Secretary, Dr. Perry R. Mandel, Nassau Hospital, Mineola, L. I., N. Y. Meets second Tuesday of the month in February, April, June, October and December.

Los Angeles Radiological Society
Secretary, Dr. Austin R. Wilson, 540 N. Central Ave., Glendale, Calif. 91203. Meets second Wednesday of month in November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif.

Maine Radiological Society
Secretary, Dr. J. T. Chen, 7 Cherry Hill Terrace, Waterville, Me. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Henry Startzman, Medical Arts Building, Baltimore, Md.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Vernon I. Smith, Jr., Suite 203, 1085 Madison Ave., Memphis, Tenn. 38104. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. William D. Roberts, 2197 Los Arrow Dr., Dayton 9, Ohio. Meets second Friday of fall and winter months.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Alexander W. Friedman, Mid-Hudson Medical Group, Fishkill, N. Y. Meets 7:00 p.m., first Wednesday of each month September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. Donald P. Babbitt, 1700 W. Wisconsin Ave., Milwaukee, Wis. 53233. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society
Secretary-Treasurer, Dr. Edward A. Peterson, St. Paul, Minn. Meets twice annually, fall and winter.

Mississippi Radiological Society
Secretary-Treasurer, Dr. Dan T. Keel, Jr., 504 Chippewa St., Brookhaven, Miss. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 p.m.

Missouri Radiological Society
Secretary-Treasurer, Dr. M. Shoss, Cape Girardeau, Mo.

Montana Radiological Society
Secretary, Dr. Clark Grimm, Great Falls, Montana. Meets at least once a year.

Nebraska State Radiological Society
Secretary, Dr. Richard Bunting, The Radiologic Center, Nebraska Methodist Hospital, Omaha 31, Neb. Meets third Wednesday of each month at 6 p.m. in Omaha or Lincoln.

Nevada Radiological Society
Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

New England Roentgen Ray Society
Secretary, Dr. Jack R. Dreyfuss, Zero Emerson Place, Boston, Mass. 02114. Meets third Friday of each month, October through April, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 p.m.

New Hampshire Roentgen Ray Society
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New Mexico Association of Radiologists
Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

New Mexico Society of Radiologists
Secretary, Dr. William G. McPheron, Hobbs, New Mexico. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New York Roentgen Society
Secretary, Dr. Harry Z. Mellins. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 p.m.

North Carolina Radiological Society
Secretary, Dr. E. H. Schultz, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. Robert J. Olson, 1240 8th Ave., Williston, N. D. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Anthony J. Tabacco, 621 Central Ave., Albany 6, N. Y. Meets in Albany area on second Wednesday of October, November, March and April.

Northern California Radiological Society
Secretary-Treasurer, Dr. John Turner, 1215-28th St., Sacramento, Calif. Meets fourth Monday of Sept., Nov., Jan., March and May at the Sutter Club in Sacramento.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society
Secretary, Dr. Mortimer Lubert, Cleveland, Ohio. Annual meeting: Toledo, Ohio, May 13–15, 1966.

Oklahoma State Radiological Society
Secretary, Dr. Robert Sukman, 1200 N. Walker, Oklahoma City, Okla. Meets in January, May and October.

Orange County Radiological Society
Secretary-Treasurer, Dr. Herbert H. Benson, 100 East Valencia-Mesa Dr., Fullerton, Calif. Meets fourth Tuesday of every month in Orange County Medical Association Building.

Oregon Radiological Society
Secretary-Treasurer, Dr. Robert S. Miller, 13753 S.W. Farmington Rd., Beaverton, Ore. 97005. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary-Treasurer, Dr. Willis Taylor, 1118 9th Ave., Seattle, Washington. Annual meeting to be announced.

Pennsylvania Radiological Society
Secretary, Dr. T. Frederick Weiland, Jr., 619 Ridgeway Ave., Grove City, Pa. Annual meeting: Hotel Hershey, May 12–14, 1966.

Philadelphia Roentgen Ray Society
Secretary, Dr. C. Jules Rominger, Misericordia Hospital, 54th St. and Cedar Ave., Philadelphia, Pa. 19143. Meets first Thursday of each month at 5 p.m., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Robert N. Berk, 3305 Fifth Ave., Pittsburgh 13, Pa. Meets second Wednesday of month, October through June at Park Schenely Restaurant.

Radiological Society of Connecticut
Secretary-Treasurer, Dr. Orlando F. Gabriele, 1450 Chapel St., New Haven 11, Conn. Meetings are held bimonthly.

Radiological Society of Greater Cincinnati
Secretary, Dr. Harold N. Margolin, 6159 Tulane Road, Cincinnati, Ohio. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Greater Kansas City
Secretary, Dr. J. Stewart Whitmore, 1010 Rialto Bldg., Kansas City, Mo. Meets last Friday of each month.

Radiological Society of Hawaii
Secretary, Dr. Russell E. Graf, P.O. Box 294, USA Tripler General Hospital, Honolulu, Hawaii. Meets third Monday of each month at 7:30 p.m.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. Andrew F. Giesen, Ochsner Clinic, New Orleans 15, La. Meets annually during Louisiana State Medical Society meeting.

Radiological Society of New Jersey
Secretary, Dr. E. Arthur Kratzman, 912 Prospect Ave., Plainfield, N. J. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of Rhode Island
Secretary-Treasurer, Dr. Harvey B. Lesselbaum, Miriam Hospital, Providence, R. I.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester 18, N. Y.

Radiological Society of South Dakota
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Gerald M. McDonnel, U.C.L.A. Medical Center for Health Sciences, Los Angeles, Calif. 90024. Meets three times a year, usually October, February, and May.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Irving B. Joffe, Rochester General Hospital, 1425 Portland Ave., Rochester 21, N. Y. Meets at 8:15 p.m. on the last Monday of each month, September through May, at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. John H. Freed, 4200 East Ninth Ave., Denver 20, Colo. Annual meeting to be announced.

San Antonio-Military Radiological Society
Secretary, Dr. Hugho F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Tex. Meets third Wednesday each month in Fort Sam Houston Officer's Club at 6:30 p.m.

San Diego Radiological Society
President-Secretary, Charles P. Hyslop, 7901 Frost St., San Diego 22, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary, Dr. Malcolm Jones, University of California Hospital, San Francisco 22, Calif. Meets quarterly at the San Francisco Medical Society, 250 Masonic Ave., San Francisco 18, Calif.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. George T. Hennessey, Washington, D. C. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 p.m.

Section on Radiology, Southern Medical Association
Secretary, Dr. Andrew F. Giesen, Jr., White-Wilson Clinic, Fort Walton Beach, Fla. Annual meeting: Houston, Texas, Nov 1–4, 1965.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

Shreveport Radiological Club
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

Society for Pediatric Radiology
Secretary, Dr. John L. Gwinn, Children's Hospital, Los Angeles 27, Calif. Annual meeting: Washington Hilton Hotel, Washington, D. C., September 27, 1965.

Society of Nuclear Medicine
Secretary, Mr. C. Craig Harris, Oak Ridge National Laboratories, Oak Ridge, Tenn. *Administrator*, Mr. Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill. Annual meeting to be announced.

South Bay Radiological Society
Secretary, Northern Section: Dr. John H. Callaghan, 2900 Whipple Ave., Redwood City, Calif.; Southern Section: Dr. Carleton J. Wright, 2015 Clarman Way, San Jose, Calif. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

South Dakota Radiological Society
Secretary, Dr. Donald J. Peik, 1417 S. Minnesota Ave., Sioux Falls, S. Dak. Meets in spring with State Medical Society and in fall.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. Annual meeting: Grand Hotel, Point Clear, Ala., Jan. 28–30, 1966.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society
Secretary-Treasurer, Dr. E. K. Carter, Holston Valley Community Hosp., Kingsport, Tenn. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas Radiological Society
Secretary, Dr. Herman C. Sehested, 815 Medical Arts Bldg., Fort Worth 2, Tex. Annual meeting: Driscoll Hotel, Corpus Christi, Jan. 28–29, 1966.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor, Mich.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society
Secretary, Dr. Carlisle C. Smith, Salt Lake General Hospital, 2033 S. State St., Salt Lake City, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society
Secretary, Dr. John R. Williams, 160 Allen St., Rutland, Vt.

Virginia Radiological Society
Secretary, Dr. John M. Ratliff, Mary Immaculate Hospital, Newport News, Va.

Washington State Radiological Society
Secre ary, Dr. Owen Marten, 930 Terry Avenue Seattle, Wash. Meets quarterly.

West Virginia Radiological Society
Secretary, Dr. Karl J. Myers, The Myers Clinic-Broaddus Hospital, Philippi, W. Va. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester Radiological Society
Secretary, Dr. Peter P. Brancucci, Westchester Academy of Medicine, Section on Radiology, Purchase, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. Charles Benkendorf, 408 St. Francis St., Green Bay, Wis. Meets twice a year, May and September.

Cuba, Mexico, Puerto Rico and Central America

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Roberto Calderón, Calle Central Oeste No. 218, Managua, Nicaragua, Central America. Meets annually in a rotating manner in the six countries.

Sociedad de Radiología de El Salvador
Secretary, Dr. Rafael Vaga Gómez.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad de Radiología y Fisioterapía Cubana
Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba. Meets monthly at Curie Hospital.

Sociedad Costarricense de Radiologia
Secretary, Dr. James Fernández Carballo, Apartado VIII San José, Costa Rica.

Sociedad Mexicana de Radiología, A.C.
Calle del Oro No. 15, México 7, D. F.
Secretary-General, Dr. E. Alvarez Hernández.
Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Jorge Carreras Girard, Suite 504, Professional Bldg., Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. R. D. Hoare, 32 Welbeck St., London, W. 1, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics.
Honorary Secretary-Treasurer, Paul M. Pfalzner, Dept. of Therapeutic Radiology, University of Western Ontario, London, Ont., Canada. Annual meeting to be announced.

Edmonton and District Radiological Society
Secretary, Dr. J. T. Mason, 540 Tegler Bldg., Edmonton, Alberta, Canada. Meets second Tuesday of each month, October to May.

Faculty of Radiologists
Honorary Secretary, Dr. J. N. Pattinson, 47 Lincoln's Inn Fields, London, W.C.2, England. Annual meeting to be announced.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal

Society of Medicine, 1 Wimpole St., London, W. 1, England.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. D. J. Sieniewicz, *Associate Honorary Secretary-Treasurer*, Dr. Maurice Dufresne, 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual meeting to be announced.

Montreal Radiological Study Club
Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Jacques Lespérance, 1656 Sherbrooke East, Montreal, Que., Canada. Meets every third Tuesday from October to April. Annual meeting: Montreal, Que., Canada, Dec. 8–11, 1965.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

College of Radiologists of Australasia
Honorary Secretary, Dr. E. A. Booth, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 p.m. in the Hospital Nacional de Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Tede Eston de Eston, Caixa Postal 5984, São Paulo, Brazil.

Sociedad Argentina de Radiologia
Secretary, Dr. Armando B. de Onaindia, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Bolivana de Radiología
Secretary, Dr. Javier Prada Méndez, Casilla 1596, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Nicola Caminha, Av. Mem. de Sa, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. J. P. Velasco, Avenida Santa María 0410, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary, Dr. Armando Uribe, Hospital Miltar Central, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Luis Blum, P.O. Box 3712, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary, Dr. Vicente Ubillus, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta 218, Lima.

Sociedad de Radiológica del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41–110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiologia.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. Ernesto H. Cibils, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiologia de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenologia y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Carlos A. Oulton, Santa Rosa 447, Córdoba, Argentina.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Luis F. Muro, Apartado No. 9362 Candelaria, Caracas, Venezuela. Meets monthly third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik. Annual meeting to be announced.

Société Belge de Radiologie
General Secretary, Prof. Simon Masy, Louvain, Belgium. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Permanent Secretary, Dr. Jaques Sauvegrain, Hôpital des Enfants-Malades, 149, rue de Sèvres, Paris 15e, France.
General Secretary, Dr. Ole Eklöf, P.O. Box, Stockholm 60, Sweden. Annual meeting to be announced.

Société Française d'Électroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru, Paris 8e, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Srobárova 50, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Deutsche Röntgengesellschaft
Secretary, Professor Dr. med. H. Lossen, Universitäts-Röntgeninstitut, Lagenbeckstr. 1, Mainz, Germany.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano, Torino, Italy. Meets annually.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. H. F. O. Stricker, Schalklaar, Netherlands.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Española de Radiología y Electrología Médicas y Medicina Nuclear
Secretary, Dr. D. Aureo Gutierrez Churruca, Esparteros, No. 9, Madrid, Spain. Meets monthly in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

Indonesian Radiological Society
Secretary, Professor Sjahriar Rasad, Taman Tjut Mutiah 1, Diakarta, Indonesia.

ABSTRACTS OF RADIOLOGICAL LITERATURE

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ROENTGEN DIAGNOSIS

Genitourinary System

Faegenburg, David, Bosniak, Morton, and Evans, John A. Renal sinus lipomatosis: its demonstration by nephrotomography. *Radiology*, Dec., 1964, *83*, 987–998. (From: Departments of Radiology, The Mount Sinai Hospital, Montefiore Hospital, and The New York Hospital Cornell Medical Center, New York, N. Y.)

Renal sinus lipomatosis is the accumulation of excessive nontumorous fatty tissue within the renal sinus. In the course of normal aging, the thin layer of loose fatty tissue enveloping the pelvocalyceal and vascular structures undergoes a slight, gradual increase and under extraordinary conditions the amount of fat in the renal sinus is so excessive that pelvocalyceal deformity results. Massive obesity is the most frequent cause but proliferation of fat also occurs when there is loss of renal parenchyma as a result of infection, infarction, or arteriosclerotic ischemia. While innocuous in its effect on the patient, its main clinical importance is due to the pelvocalyceal deformities which suggest renal tumors or cysts.

Plain roentgenography of the kidney regions and plain tomography may show the excessive fat in the renal sinus. Excretory urography usually well demonstrates the deformities caused by lipomatosis. These deformities consist of elongation, arcuate curvature, and "squeezing" of the infundibula, resulting in a spidery appearance of the pelvocalyceal system. Nephrotomography, however, usually permits the making of this diagnosis with confidence. Oblique body-section roentgenograms obtained during the nephrogram phase show the characteristic findings. The fatty tissue, being relatively avascular and of less than water density, is seen as a translucent zone, outlined peripherally by opacified renal parenchyma and centrally by the calyces and pelvis. A finding of great specificity is the visualization of tongues of opacified renal cortex, the columns of Bertini, projecting into the lucent zone at many points, imparting a coarse saw-toothed pattern. In the instances where the fat deposition is localized, the main differential diagnosis is between focal lipomatosis and peripelvic cysts. The focal fat collection will show a variable shape with vague margins, while the cyst usually presents a perfectly round or oval shape with sharp and distinct margins.

The authors discuss the anatomy of the renal sinus, their nephrotomographic technique, and the material used in this study. They also present their classification of lipomatosis based on the distribution of fat within the sinus and the degree of parenchymal atrophy present. Many roentgenograms are reproduced illustrating the findings in this entity.—*Donald N. Dysart, M.D.*

Yulis, George P., Morrin, Peter A. F., Mackie, Kenneth W., and Bruce, Andrew W. Intravenous urography in the presence of uremia. *Surg., Gynec. & Obst.*, April, 1965, *120*, 810–816. (From: Departments of Urology, Medicine and Radiology, Queen's University, Kingston, Ontario, Canada.)

On the basis of experiments on 5 groups of dogs, the authors have demonstrated a lack of correlation between visualization of upper collecting structures by intravenous pyelography and the level of the blood urea nitrogen.

Utilizing sodium and methylglucamine diatrizoate for intravenous pyelography as well as numerous renal function studies (blood urea nitrogen, plasma, creatinine, inulin, para-amino hippuric acid, and free water clearances, and maximum renal concentration test), the authors investigated the following situations: Group 1, ureteroduodenal transplantation; Group 2, partial infarction of a kidney; Group 3, ligation and subsequent release of a ureter; Group 4, production of pyelonephritis; and Group 5, roentgen irradiation of one kidney. Despire marked elevation of blood urea nitrogen (Group 1), reduced renal function (Groups 2 and 3), and destruction of nephrons (Groups 4 and 5), good opacification by intravenous pyelography was secured in all.

The triiodide compounds are excreted almost entirely by glomerular filtration. Hence, their concentration is dependent upon glomerular filtration rate, tubular secretory rate, and amount of water removed from plasma filtrate.

The reasons for carrying out these specific experiments are given. If the glomerular filtration rate is normal, elevation of the blood urea nitrogen should not affect renal visualization (Group 1). If filtration is reduced by destruction of a portion of a kidney, the remaining intact nephrons should be visualized (Group 2). If opacification is not clearly dependent upon concentration mechanisms and intactness of nephrons, then opacification should occur despite damage to these mechanisms and to nephrons (Groups 3, 4, and 5).

These studies are in accord with other work which has revealed opacification despite functional impairment.

The results of these experiments are contrary to clinical experience in renal disease. The reason for this difference, the authors explain, is that the renal concentrating mechanism of the dog is far superior to that of man.—*Justin J. Wolfson, M.D.*

Nervous System

Korein, Julius, Kricheff, Irvin I., Chase, Norman E., and Randt, Clark T. Computer processing of neuroradiological reports: an introduction to the application of the variable-field-length format and Medtran.

Radiology, Feb., 1965, *84*, 197–203. (From: Departments of Radiology [Neuroradiology] and Psychiatry and Neurology, New York University Medical Center, New York, N.Y.)

A method of writing radiologic reports and simultaneously transcribing the report into machine language for computer input has been devised. The method utilizes a special commercially available typewriter which will type a routine radiologic report and at the same time punch a paper tape. The type is then used for computer input, storage, and analysis.

The radiologist receiving the system must be familiar with the format, as must the typist. Dictation is done according to a rigid format in fixed sequence. The format is divided into two sections, with the first termed the fixed-field for statistical and identifying data; the second section, termed the variable-field, contains the description of the procedure and radiographic findings. The amount of data that can be placed in this second section is almost unlimited. After the report is typed it is edited, any needed corrections made, and the information transferred to magnetic tape.

Once the data are stored on magnetic tape, many procedures can then be done utilizing the information. Uses include retrieval of a specific report, printing out all reports with a specific finding, age grouping and many others. Other factors to be considered in the use of this program include cost, with the typewriter price being $1,500 to $3,000. About 4,000 pages of narrative reports may be stored on one reel of magnetic tape. This one reel can be analyzed for 16-variables in an hour at a cost of about $35.00 for use of the computer.

The legal status of a computer-stored report is uncertain at this time and must be considered in the future. Advantages include permanent storage in a small space of a large number of records with easy retrieval and statistical analysis. Research analysis can be both fast and simple and patterns in disease ascertained.—*James C. Moore, M.D.*

Nagel, Donald A., Albright, James A., Keggi, Kristaps J., and Southwick, Wayne O. Closer look at spinal lesions: open biopsy of vertebral lesions. *J.A.M.A.*, March 22, 1965, *191*, 975–978. (Address: Dr. Nagel, 333 Cedar Street, New Haven, Conn.)

A review of 254 patients admitted to a University Orthopedic Surgery Service indicated that at least 1 out of 10 patients had underlying pathology which was not responsive to the usual conservative treatment of bed rest and analgesics. This 10 per cent consisted of 8 per cent who had lesions due to an infectious process and 2 per cent who had neoplastic lesions.

Open surgical biopsy of the vertebral lesion is recommended over the closed needle biopsy because localization is more accurate with open biopsy and because more material can be obtained for culture and histologic study. Open biopsy has also, on occasion, provided a method of immediate treatment, as with drainage of a psoas abscess.

A posterolateral, modified costotransversectomy approach was usually employed, with roentgenograms utilized during the procedure to verify the exact level. The lesion was then curetted under direct visualization.

If a rather extensive destructive lesion is present in the vertebral body, an anterior, anterolateral, or lateral exposure is recommended rather than the posterior route, since posterior laminectomy in this circumstance may result in removal of the only remaining skeletal outline for the spinal cord.

When indicated, open surgical biopsy provided a very helpful guide to treatment, establishing an accurate histologic diagnosis and allowing prompt institution of a specific therapy. There have been no undesirable sequelae to date.—*Donald M. Monson, M.D.*

SKELETAL SYSTEM

Bullough, Peter G., Kambolis, Catherine P., Marcove, Ralph C., and Jaffe, Henry L. Bone infarction not associated with caisson disease. *J. Bone & Joint Surg.*, April, 1965, *47A*, 477–491. (From: Laboratory Division, Hospital for Joint Diseases, New York, N. Y.)

The authors describe 19 cases of bone infarction in areas other than the femoral head. Excluded were patients with caisson disease, sickle cell anemia, osteochondritis dissecans and other osteochondritides. A pathologic examination was carried out in each case.

Sexual distribution was almost equal. The average age at the time of diagnosis was 50 in the men and 45 in the women with an age span of 21 to 72 years. In approximately one-half of the cases, pain was present and was attributed to the bone infarction. In the other patients, the infarction was an incidental finding.

In 13 patients only one bone was involved roentgenographically; in the other 6, more than one bone was involved. In 2 cases there was symmetric bilateral involvement. Long bones were more frequently affected, with the upper tibia and lower femur the most common sites. In the long bone lesions, the infarction was situated principally in the metaphyses. Involvement of the ilium was present in 3 patients. Other sites of involvement were the rib in 1 case and the os calcaneus in 2 cases.

In the acute infarction no roentgenographic changes are present. Later, a connective tissue rim forms about the periphery of the lesion. As this rim becomes infiltrated with calcium salts, the central portion of the lesion undergoes necrosis, forming a cystic lesion with a dense periphery roentgenographically. The central portion eventually contains flecks of calcification. The most frequent roentgenographic interpretation was some type of benign bone neoplasm, usually thought to be enchondroma.

Arterial embolization as an etiologic mechanism seemed unlikely in most of the cases as did a generalized vascular disease. Probably, more than one etiologic mechanism is implicated.—*Gerald Barry, M.D.*

Dresher, Charles S., and Macdonell, James A. Total amelia. *J. Bone & Joint Surg.*, April, 1965, *47A*, 511–516. (From: Area Child Amputee Center [Michigan Crippled Children Commission], 920 Cherry Street, Grand Rapids, Mich.)

The authors review the world literature on total amelia. They consider only 11 of the 27 cases reported as quadrimembral amelia.

Two additional cases are reported here, one of which died at 4 days while the other is alive and well at the end of 7 years.

At the present time this 7 year old girl has a plastic bucket with Canadian-type hip joints and single pivot knee joints and S.A.C.H. feet. She is able to stand for prolonged periods and to walk independently, although laboriously and precariously, at a marginal functional level.

The child also has bilateral shoulders disarticulation prostheses with a universal shoulder joint, elbow lock, friction turntable at the elbow, fraction wrist unit, wrist-flexion unit, and a voluntary opening terminal device. She is able to feed herself, draw, and write.

The description of the various devices used since birth is of interest.—*C. Peter Truog, M.D.*

Sherman, Mary S., and McFarland, Gordon, Jr. Mechanism of pain in osteoid osteomas. *South. M. J.*, Feb., 1965, *58*, 163–166. (From: Ochsner Foundation Hospital, New Orleans, La.)

Histologic sections of 21 osteoid osteomas revealed definite evidence of unmyelinated nerves in 15 cases; 5 cases showed structures which were almost certainly nerves; no nerves were seen in the remaining cases. In general, the nerves were found singly or in clusters in the fibrous zones surrounding the nidus, usually accompanying one or more blood vessels.

The proposed explanation for not finding nerve tissue in the nidus itself is that the nerves are probably so small in caliber that they are lost in the tangle of cellular elements and vascular components of the nidus. Silver stains provided no further assistance here. In general, the nerves visualized on microscopic section were found running parallel to the long axis of the bone.

Since osteoid osteomas are extremely vascular lesions and an abundant nerve supply has been seen in most of these lesions, the authors postulate that the nerves arrived with the vessels. The changing pressure of the highly vascular lesion stimulates these visceral afferent nerves and gives rise to the "characteristic pain."—*Ronald Schaupp, M.D*

Muggia, Franco M., and Tennant, Robert. Osteogenic sarcoma of the ilium: report of a case associated with osteoblastic prostatic adenocarcinoma. *J. Bone & Joint Surg.*, April, 1965, *47A*, 500–510. (From: Hartford Hospital, 80 Seymour Street, Hartford 15, Conn.)

The authors report a 66 year old man in whom an osteogenic sarcoma arose in the ilium without evidence of pre-existing Paget's disease. On the initial roentgenogram of the pelvis, a lytic lesion was present in the superior portion of the left ilium. The lesion was found to have increased in size on a roentgenogram after 6 months and osteoblastic metastases not present on the previous study were also seen.

Necropsy performed 7 months later disclosed lung and pleural metastases from the osteogenic sarcoma but also an unsuspected adenocarcinoma of the prostate with metastases to bone.

The authors offer the suggestion that metastases from the adenocarcinoma of the prostate stimulated the development of an osteogenic sarcoma through the osteoblastic effect on bone of the metastases. This theory, as well as others, is developed at some length.—*Gerald Barry, M.D.*

Chung, Stanley M. K., and Janes, Joseph M. Diffuse pigmented villonodular synovitis of the hip joint; review of the literature and report of four cases. *J. Bone & Joint Surg.*, March, 1965, *47A*, 293–303. (Address: 200 First Street, S. W., Rochester, Minn.)

The 4 new cases of diffuse pigmented villonodular synovitis of the hip joint reported by the authors and the 13 other cases collected from the English language literature reveal that this disease is most common in females in their fourth and fifth decades of life, with the duration of symptoms averaging several years. The typical symptoms include increasing pain in the involved hip and a limp. In all cases the disease was monarticular, and there were no systemic symptoms or abnormal laboratory findings.

The predominant roentgenographic findings were multiple cystic areas in the acetabulum and the femoral head and neck, a narrowed but preserved joint space, an occasional diffuse sclerosis of the femoral head, and an occasional distention of the hip joint capsule. No marked distortion of the contour of the femoral head comparable to that commonly seen in advanced osteoarthritis was noted.

The differential diagnosis includes osteoarthritis, avascular necrosis, tuberculous arthritis sicca, monarticular rheumatoid arthritis, synovial sarcoma, chondrosarcoma, metastatic carcinoma, and gout.

Needle biopsy with aspiration of the characteristic serosanguineous fluid and tissue is suggested as the best method, short of open biopsy, to substantiate the diagnosis.

Recommended treatment is meticulous synovectomy and grafting of the cysts combined with cup arthroplasty. Occasionally, an Austin-Moore prosthesis is indicated when there is marked destruction of the femoral head. Radiotherapy is of no apparent benefit initially, but might be considered with any recurrences.—*Donald M. Monson, M.D.*

Howorth, Beckett. The etiology of congenital and infantile displacement of the hip. *Acta orthop. scandinav.*, 1965, *35*, 212–224. (Address: 49 Lake Avenue, Greenwich, Conn.)

The displacements of the fetal or infant hip are considered by the author to be secondary to an elongated capsule and secondary mechanical forces. He has found that with displaced hips (subluxations and dislocations) acetabular deformity is not always present, and when present is not proportional to the degree of the displacement. There may be no acetabular dysplasia despite complete dislocation. The location and degree of exerted pressure determine the type and degree of deformity. If a subluxation persists, the pressure of the head against the margin of the acetabulum results in a permanent obliquity. Anteversion is not always present.

Normal fetal hips were studied and it was found that lateral hip displacement was prevented by a normal capsule and when this was cut the hips would subluxate. Hip displacement was not found in embryo specimens but rather during fetal development or after birth.

The author has seen over 200 patients with hip displacements in the last 25 years. In every case he found relaxation of the ligaments of the fingers, wrists, elbows and knees. In 121 hips having surgery, the capsule was found to be elongated in every instance and this was the only pathologic finding common to all cases. In 54 per cent of the hips, simple open reduction with correction of the capsular elongation gave excellent results. Primary acetabular dysplasia was not found to be the cause of hip displacement.—*Martha Mottram, M.D.*

Rubin, Gustav, and Witten, Morris. The unstable ankle. *Bull. Hosp. Joint Dis.*, Oct., 1964, *25*, 179–190. (From: Veterans Administration Outpatient Clinic, Brooklyn, N. Y.)

The laterally unstable ankle is the one that "turns over" readily, frequently resulting in sprain.

Investigation of the unstable ankle must take into account the following: (1) the ligament stabilizing the ankle joint; (2) the ligament stabilizing the subtalar joint; (3) the muscles acting on the lateral foot and ankle; (4) the alignment of the bony components of the ankle; (5) factors not related to the stabilizing musculo-skeletal structures; and (6) other causes of instability.

The authors report that more than half of the normal ankles they have examined revealed a talar tilt of 3° to 23° and that more than 20 per cent showed a difference in talar tilt between the two ankles of the same individual. Sedlin found that the maximum variation between the right and left ankles in normal subjects is 10°. With these findings in mind, the surgeon should not accept small amounts of talar tilt as evidence of ankle instability. The clinical evaluation of the patient should be the deciding factor.

The stability of the subtalar joint was evaluated by use of an angle bar device and laminagraphy in the frontal plane. The usual range of the tibiocalcaneal inversion angle was 30° to 50° with little difference between the two sides after correction for talar tilt. The authors correlated clinical hypermobility with angles approaching and exceeding 50°. Patients with gross peroneal weakness often complain of frequent turning over of the ankle. When weakness of this muscle is severe enough to allow turning over, it is evident clinically and there appears to be no need for roentgenologic evaluation.

Although several cases of severe genu varum were examined, no cases of instability were encountered. The subtalar joint appears to compensate for the upward and inward slope of the ankle joint associated with this.

Of the causes not related to the stabilizing musculo-skeletal structures, the patient with the high medial arch support and worn down lateral heel is probably the most common example.

This report does not deal with the talar tilt of acute injuries.

Conservative treatment may consist of lateral shoe wedges, anklets, out-flare, heels, or the wearing of high top shoes with a medial strut. Watson Jones' reconstruction surgery may be employed but surgical treatment is very rarely indicated.—*David Morse, M.D.*

Kleiger, Barnard, and Barton, Jerome. Epiphyseal ankle fractures. *Bull. Hosp. Joint Dis.*, Oct., 1964, *25*, 240–245. (From: Hospital for Joint Diseases and The Leo Mayer Orthopaedic Group, New York, N. Y.)

Fractures of the tibial and fibular epiphyses at the ankle joint may take place at any time from birth until the epiphyseal plate has closed in adolescence.

Aiken described three types of epiphyseal fractures: Type I. An avulsion of the entire epiphysis usually with a metaphyseal spike. Displacement may be marked. Type II. An incomplete undisplaced fracture of the epiphysis not involving the epiphyseal plate. This is due to a mild compression force. Type III. A fracture through the epiphysis crossing the epiphyseal plate. This is due to a vertical compression force and may or may not be displaced.

Lateral rotation is the most frequent cause of ankle injury and tibial epiphyseal fracture, due to this, usually involves the entire plate with a posterior triangular metaphyseal spike which remains attached to the epiphysis. The epiphyseal fragment is usually displaced laterally or posteriorly.

In eversion, the talus strikes and compresses the lateral portion of the tibial epiphysis. It may also fracture or tear the tibio-fibular ligaments and widen the syndesmosis.

In inversion, the talus strikes the tibia at the mortise angle and fractures the epiphysis vertically. The fracture may cross the plate to involve the metaphysis. This mechanism may tear the lateral ligaments and cause inversion instability or fracture of the fibular epiphysis.

Although the most common ankle fracture in the adult is fibular fracture, this is less common in a child because the fibula is much more mobile. Lateral motion, inversion or eversion, may fracture the fibular epiphysis transversely across the plate.

The prognosis of epiphyseal fracture can be predicted when the nature of the injury is known. If the fracture is due to traction, the entire tibial or fibular epiphysis or a fragment of it is avulsed. When this fracture is reduced, normal growth may be expected. If the fracture is incompletely reduced, subsequent growth may correct the malposition. The prognosis for this type of fracture is good.

Lateral thrust of the talus may push off either the medial or lateral malleolus. These fractures usually heal without difficulty and the prognosis is good.

Vertical compression does not always carry the same good prognosis. If it causes an incomplete fracture that does not involve the plate, the prognosis is good. If the epiphyseal plate is fractured, it will heal with bony callus. If the callus is wide enough or strong enough, growth is retarded at that site. Since the rest of the epiphysis continues to grow, asymmetric growth and deformity will result.—*David Morse, M.D.*

HARALDSSON, STEFAN. Pes plano-valgus staticus juvenilis and its operative treatment. *Acta orthop. scandinav.*, 1965, *35*, 234–256. (From: Orthopaedic Clinic, Lund, Sweden.)

Pes plano-valgus juvenilis is the commonest deformity of the foot. It is believed to be due to a disproportion between the strength of the muscles and ligaments and the weight carried. Most cases respond to conservative treatment, but when there is no improvement, structural changes may result with increased symptoms.

The author operated on 54 growing feet, all of which had failed to respond to conservative therapy. The purpose of the operation was to correct and prevent pronation-abduction of the loaded calcaneus with placement of bone blocks in the tarsal sinus. In some cases he also transposed the insertion of the tibialis anterior tendon to the navicular. Fixation of the distal end of the graft to the calcaneus was the only fixation desired.

The preoperative treatment in his cases averaged 4 years; the average age at time of surgery was 6.3 years. In all cases the condition was bilateral and 55 per cent had symptoms. Results of surgery were good in 74 per cent, improved in 19 per cent, and poor in 7 per cent.

At follow-up examination pedographs, photographs and roentgenograms of the arch and loaded heel were taken with measurement of the angle between the axis of the talus and the floor (TF angle average 23 degrees). The "before and after" studies are presented in 7 heels.

There was no indication that growth disorders resulted from surgery. The operation should be performed early enough to secure normal development of the growing bones before deformity is irreversible; surgery before age 12 is therefore indicated.—*Martha Mottram, M.D.*

STØREN, H. Congenital ankylosis of the elbow: late results in one operated case with bilateral ankylosis. *Acta orthop. scandinav.*, 1965, *35*, 202–211. (From: Coast Hospital at Stavern, Norway.)

The author reports a case of congenital bilateral ankylosis of the elbow in a patient with other congenital bone and joint defects. On the right there was a broad synostosis between the humerus, radius and ulna with hypoplasia of the ulna. On the left there was a broad synostosis between the radius and humerus; the proximal end of the ulna was deformed and separated by a cleft from the humerus.

The author states that in all of the previously reported cases except 1, the radius has been the chief bone in the formation of the ankylosis. No epiphyseal lines were evident in the bones at the elbow.

The patient had surgery on the right elbow at 4½ months and 2 additional arthroplasties at 8 years because of re-ankylosis. The left elbow had surgery at 1 year. Follow-up at age 14 showed limited flexion and extension but sufficient for daily needs. Two of his previous cases (4 elbows) had poor results.

He recommends surgery in all cases regardless of age, but prefers to treat them in early childhood because muscle atrophy will occur and the presence of muscles is important for a successful operative result.—*Martha Mottram, M.D.*

Fleischer, Horst. Die Arthrographie des Daumengrundgelenkes. (Arthrography of the base joint of the thumb.) *Röntgen Blätter*, Feb., 1965, *18*, 64–66. (Address: Chirurgische Klinik und Poliklinik der Berufsgenossenschaftlichen Krankenanstalten "Bergmannsheil," 463 Bochum, Germany.)

Injuries to the base of the thumb may limit mobility in the metacarpophalangeal joint and interfere with the usefulness of the entire hand. If the capsule is intact, the injection of 0.5 cc. of urografin or perabrodil will cause pain because of stretching of the capsule. If the capsule is torn, 1.0 cc. of the contrast material will spread beyond the confines of the capsule and delineate the para-articular soft tissues. Thus a rupture of the fibro-cartilaginous band on the volar aspect of the joint can be diagnosed. At the same time, the routine roentgenograms will indicate any existing fractures in this region.

Appropriate therapeutic measures can be taken according to the findings. The author recommends a circular cast for 6 weeks in the presence of a rupture of the volar band.—*J. Zausner, M.D.*

BLOOD AND LYMPH SYSTEM

Gillanders, Lewis A., and Strachan, R. W. The role of radiology in the diagnosis of Takayasu's arteriopathy ("pulseless disease"). *Clin. Radiol.*, April, 1965, *16*, 119–129. (From: The Royal Infirmary, Aberdeen, Scotland.)

In 1908 the Japanese ophthalmologist Takayasu described the striking appearances of advanced chronic ischemic retinopathy observed in a young woman. These retinal abnormalities were found to occur in the presence of severe bilateral stenosis of the vessels arising from the aortic arch. It is seen most often in adolescent and young adult females, and only occasionally in males. Early and late phases of the disease with extremely variable clinical features are recognized. In the early phase there are systemic symptoms similar to those of systemic lupus erythematosus. This phase is characterized by such symptoms as fever, night sweats, arthralgia, myalgia, cough, hemoptysis, pleurisy, pleural effusion, anemia, pericarditis, aortitis, aortic incompetence, leg ulceration, neck and abdominal arterial bruits and persistent erythrocyte sedimentation rate elevation. Roentgenologic examination in this phase of the disease may reveal segmental dilatation of the thoracic aorta. The recognition of an aortitis is the important clue which may allow the diagnosis of Takayasu's arteriopathy to be suggested on the basis of the chest roentgenogram alone.

During the late occlusive or pulseless phase, arterial stenosis may cause the stroke syndrome, superior mesenteric artery stenosis, renal artery stenosis or intermittent claudication. Roentgen examination may reveal not only evidence of thoracic aortitis, but also rib notching and calcification of the descending thoracic or abdominal aorta. Contrast roentgenography of the entire aorta and its major branches is required to define the exact extent and character of existing arterial abnormalities. This will permit a decision as to the advisability of using cortico-steroid drugs, anticoagulant therapy and surgery in treating the individual case.

Three case histories are included in this article.—*Samuel G. Henderson, M.D.*

Joffe, N. Aortitis of obscure origin in the African. *Clin. Radiol.*, April, 1965, *16*, 130–140. (From: Diagnostic X-Ray Department, Baragwanath Hospital, Johannesburg, South Africa.)

A rather unusual lesion of the aorta has been observed in African children and adolescents. This lesion is an aortitis of obscure origin, characterized by a marked irregularity of the aorta, with areas of aneurysmal dilatation and/or stenosis of varying length and degree. The etiology of the aortitis is obscure. Syphilis, tuberculosis or any known infective or toxic agent has not been found responsible. Patients usually present with severe hypertension, hypertensive encephalopathy or cardiac failure. Absence or diminution in volume of peripheral pulse may be found, clinically simulating aortic coarctation. Chest roentgenologic examination usually reveals cardiomegaly, mainly due to left ventricular enlargement. Enlargement, aneurysmal dilatation or irregularity in outline of the thoracic aorta may be noted.

On examination by aortography the abnormalities usually fall into: (1) the aneurysmal group, (2) the stenotic group and (3) a combined aneurysmal and stenotic group. In the *aneurysmal* group the outstanding feature is the irregularity and dilatation of the aorta and at times of the branch vessels. In cases without significant renal artery involvement, hypertension may be absent, but an important clinical finding may be a discrepancy or absence of pulses in the neck or limbs. In the *stenotic* group aortography demonstrates a lesion which is entirely or predominantly stenotic in character. The stenosis may be localized or diffuse, and it is apparently due to a combination of mural thickening and superadded thrombosis. The *combined* group consists of patients in whom aortography demonstrates segments of aneurysmal dilatation and stenosis of the aorta, with neither lesion predominating.

The main clinical problem in children and adolescents with idiopathic aortitis is the hypertension resulting from renal artery involvement. The author has seen only 1 African patient over the age of 20 years in whom the findings were suggestive of an aortitis similar to that observed in childhood and adolescent cases.

The relationship between the classic cases of Takayasu's pulseless disease and idiopathic aortitis in African patients is uncertain. Cases are encountered in which differentiation is difficult or impossible.

While all of the author's cases have occurred in African patients, the disease is not restricted to the African. A stenosing aortitis of obscure origin has been observed in India. Also, the occurrence of a "primary arteritis of the aorta causing renal artery stenosis and hypertension" has been described in Chinese patients in Singapore.

This paper includes 4 case histories of idiopathic aortitis, and 1 of Takayasu's pulseless disease.—*Samuel G. Henderson, M.D.*

WAGNER, HENRY N., JR., JONES, ELLIS, TOW, DONALD E., and LANGAN, JAMES K. A method for the study of peripheral circulation in man. *J. Nuclear Med.*, Feb., 1965, *6*, 150–154. (From: Departments of Medicine, Radiology and Surgery, The Johns Hopkins University School of Medicine, Baltimore, Md.)

Several nonradioactive methods have been used to study the peripheral circulation. The authors injected macroaggregates of human serum albumin labeled with I^{131} into the femoral artery to delineate and quantitate the distribution of radioactivity throughout the leg.

The relative distribution of the blood flow through the vessels, whose diameters are less than that of the injected aggregates, can be determined by scintillation scanning and comparing the concentration of the radioactivity from one region to another. Quantification of the radioactivity in the delineated areas can be determined by densitometric measurements of the photographic scanning image, or by integrating the counting rates as the detector is moved over the various regions.

The macroaggregates are from 10 to 100 micra in size and are trapped in the first capillary bed they encounter. No toxic or hemodynamic effects are produced due to the small quantity injected and the metabolization of the aggregates. The radioactivity disappears from the leg within 48 hours.

The authors' technique consisted of injecting 300 μc of I^{131} MMA into the femoral artery at the level of the inguinal ligament. The thyroid was blocked by a prior administration of Lugol's solution. The average count rate was determined by means of a stationary detector with a ¾ inch crystal with a flat field collimator placed 1 inch above the skin at various positions 2 inches apart, beginning at the anterior superior spine of the iliac crest. The count rate in all positions was averaged and the count rate at any site was expressed as a ratio to the average count rate.

A scintillation scan was then made of the leg. The scans showed that the distribution of the radioactivity corresponded to the distribution of the muscle masses. The thighs gave a higher count rate than the calves. The knees and ankles were relatively avascular.

Eleven studies were done, including 7 on normal males. A case of arteriosclerotic peripheral vascular disease is presented.

The above method is technically not complicated, safe, readily available and gives information previously unavailable regarding the regional muscle blood flow in the extremities under a variety of physiologic and pathologic conditions.—*Charles W. Cooley, M.D.*

GREMMEL, H. Coronarographie mittels gleichzeitiger Kontrastmittelinjektion durch zwei Katheter. (Coronary arteriography by simultaneous injection through two catheters.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Feb., 1965, *102*, 131–134. (Address: 4 Düsseldorf, Moorenstr. 5, Germany.)

Two Kifa catheters are inserted either into a femoral or axillary artery and their tips are advanced to the root of the aorta. Tiny perforations near the tips of the catheters may be made to effect a better dispersal of the contrast material in the region of the coronary ostia.

The author uses about 25–30 cc. of conray–80 as the contrast substance.

Intubation anesthesia is recommended but not essential.

Compression of both carotids during and immediately following the injection should be performed for better concentration of the contrast material in the coronary arteries. This procedure also reduces the risk of the examination.

Biplanar serial studies are made and mechanical injection pumps facilitate the study.—*J. Zausner, M.D.*

KAPLAN, LEOPOLD S., HELFF, JOHN R., and KIRCHNER, RICHARD G. The application of a pressurized infusor to arteriography. *Radiology*, Feb., 1965, *84*, 330–331. (From: Department of Radiology, Middlesex General Hospital, New Brunswick, N. J.)

Clot formation in any of the various types of needles or catheters used in arteriography has always been a troublesome factor in this procedure. The primary method of preventing such an occurrence has been the intermittent manual flushing of the needles or catheters with the standard glass syringes. This method, however, invariably produced a certain amount of movement which may be disadvantageous with certain carefully placed needles, and the possibility always exists of dislodging a small clot that may have formed at the tip of the needle or catheter between each flushing.

The authors describe a pressurized infusor which they have used in over 100 cases of arteriography without any complication. This apparatus provides a continuous flow of flushing media through either a needle or catheter to prevent any clot formation and it reduces to a minimum the movement of the needles used for the arterial punctures. The authors feel that this pressurized infusor is a valuable adjunct to arteriographic studies.—*Donald N. Dysart, M.D.*

Curry, Hiram B. A new needle for carotid angiography. *South. M. J.*, April, 1965, *58*, 445, 451, 454. (From: Department of Neurology, Medical College Hospital, Charleston, S. C.)

A new needle has been devised to reduce the trauma of direct puncture of the carotid arteries during angiography. This instrument is superior to existing ones in that two sharp stylets for entering the artery are provided—one with a short bevel and one with a short conical point—thus making it easier to push through sclerotic arterial walls and to penetrate elastic, freely movable carotid arteries. A stylet with a rounded end is substituted when the artery has been entered, assuring atraumatic threading. To prevent subintimal dissection, the rounded stylet should not be introduced immediately upon reflux of arterial blood. The needle should be withdrawn 1 or 2 mm., the needle hub depressed slightly, the rounded stylet introduced, and the needle then threaded upwards 5 to 10 mm. Since no sharp point remains in the artery during the injection period, the danger of laceration is minimized if the patient or needle moves.

The needle is 18 gauge, thin-walled, allowing maximal lumen of 1.01 mm. for an external diameter of 1.25 mm. It is 85 mm. long. It has been used in more than 1,000 carotid angiographies without morbidity or mortality due to injury of the carotid wall. It has also been used for angiography of peripheral arteries and veins without complications from trauma.—*Lois Cowan Collins, M.D.*

Beltz, L., and Thurn, P. Das Lymphogramm beim tumorösen, retroperitonealen Lymphblock. (The lymphogram in tumorous retroperitoneal lymphatic block.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, March, 1965, *102*, 278–291. (Address: Städt. Krankenanstalten, Röntgen-Radiumklinik, Goethestrasse 51, Aachen, Germany.)

Primary neoplasias of the lymphatic system cause gross enlargement of lymph nodes but no block of the lymph flow. Metastatic carcinoma, on the other hand, gives rise to complete block with development of collateral lymphatic circulation. In tumors of the genitourinary tract, including the uterus and the bladder, the iliac lymph nodes are involved, while neoplasms of the testicle, epididymis, ovaries, ureters, kidneys and adrenals spread directly to the para-aortic lymph nodes. Retrograde seeding from the deep to the superficial and from the proximal to the distal lymph nodes may also occur.

Gross enlargement of the lymph nodes only takes place in blood dyscrasias, especially in lymphosarcoma, while in metastatic carcinoma the lymph nodes barely increase in size. When the process is moderately advanced, marginal filling defects and lacunar formations develop. In the advanced stage, a whole group or chain of lymph nodes lacks filling. Simultaneously, formation of collateral vessels and extravasation of contrast material attest to a partial or total lymphatic block. The collateral channels can be retroperitoneal or they may extend to adjacent organs, especially to the bladder and kidneys. Lymphovenous anastomoses may also develop between the retroperitoneal lymph channels and the inferior vena cava as well as the portal vein. These are characterized by rapid appearance of opaque droplets in the liver and in the lungs, while the upper para-aortic lymph nodes and the thoracic duct are blocked. The various possibilities of collateral circulation are discussed in detail.

In secondary lymphedema due to retroperitoneal lymph node seeding, it is advisable to exclude venous obstruction with the aid of venography.—*Ernest Kraft, M.D.*

Desprez-Curely, J. P., Bismuth, V., and Bourdon, R. Hypoprotéinémie "idiopathique" et stéatorrhée: démonstration lymphographique d'une fistule lympho-intestinale. ("Idiopathic" hypoproteinemia and steatorrhea: demonstration of a lympho-intestinal fistula by lymphography.) *Ann. de radiol.*, 1965, *8*, 1–16. (From: Service de Radiologie de l'Hôpital Saint-Louis, place du Dr. A.- Fournier, Paris, France.)

This is the report of a female patient who for 4 years had exhibited idiopathic proteinemia, steatorrhea and edema of the lower extremities. The lymphatic origin of the syndrome was indicated by the finding of chyle in the duodenal contents, an extreme lymphopenia, and dilated lymphatics which were revealed by laparoscopy.

Bilateral lymphography was performed by the pedal approach, and a dilated network of lymphatics was discovered along the paravertebral gutters: the hepatic and perirenal collectors were grossly dilated and channels in the region of the vena cava seemed to pass the diaphragm toward the lungs. The most important element was the visualization of a lympho-intestinal fistula, with opaque material found in jejunal loops. The thoracic duct was not visualized. Surgery revealed enormously dilated lymphatics, atresia or malformation of the thoracic duct, and a lymphatic fistula into the first part of the duodenum.

This is the second case in the literature wherein a lympho-intestinal fistula explained the protein loss and associated steatorrhea in idiopathic hypoproteinemia. These cases corroborate recent information on the frequency and importance of lymphatic lesions in exudative enteropathies, which can also be secondary to compression or malignancy of lymph nodes, or primary lesions of the lymph channels of unknown origin, although possibly they come from repeated infections with sclerosis of mesenteric or abdominal lymphatics, or from congenital lesions.—*Frank A. Riebel, M.D.*

GENERAL

CAVE, L., FUSTEC, R., and BASSET, A. Radiologie de la lèpre. (Radiology of leprosy.) *Ann. de radiol.*, 1965, *8*, 61–76. (From: Hôpital Le Dantec, Dakar, Sénégal.)

The radiologic examination is a valuable means of uncovering pathology which precedes the mutilating phase of leprosy, and consists in evaluating bones, blood vessels and nerves. The present analysis is one of 210 osseous studies, 10 arteriographies and 30 neurographies.

Systematic examination of the hands and feet in cases of early leprosy while the skin is still intact will frequently uncover fine lesions due to leprous granulomas of hematogenous origin: these may be small epiphyseal geodes, pseudo-foramina, or erosions on the phalangeal tufts. Later stages of the disease exhibit osteitic lesions which have extended from open lesions, osteoarthritis, osteoporosis and osteolysis as a result of neurotrophic disorders, gross osseous destruction, involvement of facial bones, and leprous maxillary sinus.

To investigate vascular lesions, 10 arteriographies were done on the extremities of 6 patients, of whom 4 were chosen because osseous lesions were minimal or absent. Nine of the 10 studied revealed vascular damage, typical lesions being filiform networks, thromboses, and arteriovenous shunts.

To study leprous neuritis, 30 neurographies were performed on long-standing cases. The procedure consists of injecting 2 cc. of lipiodol into the ulnar nerve sheath where it lies in the sulcus nervi ulnaris, directing the needle peripherally. Roentgenograms are taken immediately, and at from 2 hours to 2 days or even later. The opaque material spreads slowly within the sheath proximally and distally; in 7 of the 30 cases visualization was obtained from axilla to wrist in 6 to 8 days. The principal pathologic finding is hypertrophy of the nerve, the caliber of which may vary sharply due to annular adhesions, and parietal alterations may be visualized.—*Frank A. Riebel, M.D.*

FLIEGEL, O. On acute soft tissue calcinosis. *Bull. Hosp. Joint Dis.*, Oct., 1964, *25*, 246–251. (From: Orthopaedic Section, V. A. Outpatient Clinic, Brooklyn, N. Y.)

Acute soft tissue calcinosis (ASTC) belongs to the dystrophic form of calcification. It is a short lived, self limited condition. It appears suddenly without prodromal signs or symptoms. It has a very acute phase and quickly disappears without residual discomfort.

There is a similarity between ASTC and acute calcific peritendinitis of the shoulder. The majority of the latter cases, however, show a natural history difference from that of ASTC. They demonstrate a definite chronicity of findings with an acme of a hyperacute phase. Unlike the ASTC, most cases of peritendinitis of the shoulder, after the acute phase has subsided, remain more or less symptomatic and the calcium deposits are still demonstrable, although they may have lost in density and may have shrunk. There are, however, some patients with calcareous peritendinitis of the shoulder who prior to the acute attack never complained about their shoulder and whose acute attack disappeared with complete dissolution of these calcific deposits. The pathogenesis of these cases seems to be different from that of the "common" calcific peritendinitis; these are cases of ASTC.

Roentgen examination reveals a calcific shadow which may be nodular, streak-like or granular, being often so minute that it is easily overlooked. The size of the calcific deposit is not always a measure of the intensity of pain. The density of the shadow is a better guide. With the gradual subsiding of the acute attack, the density fades and the shadow becomes more translucent and inconspicuous. It may take several weeks until the last traces of calcium have disappeared.

The etiology of this entity is obscure. The differential diagnosis includes the acute infectious arthritides, acute cellulitis and an acute gouty attack. The physiologic rest of the affected member supported by sedatives and analgesics is the only necessary therapeutic regimen to be followed.—*David Morse, M.D.*

KROPFF, G. F. Über Veränderungen an gelenknahen metallischen Fremdkörpern. (Complications of metallic foreign bodies lodged near a joint.) *Radiologia Austriaca*, 1964, *15*, 53–57. (Address: Krankenversicherungsanstalt der Bundesangestellten, Wickenburggasse 8, Wien VIII, Austria.)

Two cases are reported in which changes occurred many years after a metallic foreign body became embedded near a joint.

One patient, who had received a gunshot wound in 1914, began to complain of pain in 1942. By 1956, subchondral sclerosis was noted as well as "disintegration" of the metallic fragment, so that tiny pieces were dispersed within the elbow joint, which contained increasing amounts of fluid.

The other patient was accidentally struck by a straight needle, which had entered the elbow and had broken into two parts. Immediate roentgenograms showed them to be intra-articular or intracapsular and the ends of the metallic foreign bodies showed signs of fragmentation. After 28 years, further studies showed that the pieces had wandered slightly from their original positions and that their surfaces had become quite irregular. The joint had become painful and swollen.

A reference is also made to Haenisch, who reported a case of lead poisoning in a patient, who had received a gunshot wound. In this particular instance, death ensued rather abruptly.

These complications may be due to: (1) purely mechanical destruction of the cartilage by direct contact with the foreign body; (2) an oligodynamic effect on the joint tissues; and (3) chemical irritation of the synovial membrane. It is therefore advisable to remove all metallic foreign bodies in or adjacent to joints.—*J. Zausner, M.D.*

RADIATION THERAPY

Greene, D., and Lomer, P. D. The application of a 14 MeV neutron source to radiotherapy. *Proc. Roy. Soc. Med.*, March, 1965, *58*, 161. (From: Christie Hospital and Holt Radium Institute, Manchester, and Service Electronic Research Laboratory, Bladock, Herts, England.)

An experimental generator of neutrons is described in which 14 mev. neutrons are produced by accelerating deuterium ions onto a tritium target. The advantage of this reaction is that it gives a useful yield of neutrons at accelerating voltages of 100 kv. The generator gives at present an output of 10^{10} n/sec. with a target life of more than 100 hours. Design studies indicate that outputs of 10^{12} n/sec. equivalent to 50 rads/min. of roentgen rays at 50 cm. from target should be possible. Efforts are being made to obtain this output.

A steel collimator 14 inches thick has been used in the generator. The dose distribution across the edge of the neutron beam is comparable with that of orthovoltage roentgen rays. The depth dose measurements, however, are comparable with those for Co^{60} gamma rays for the same field size and source skin distance. Measurements indicate slight build-up in the first three millimeters.—*Komanduri K. N. Chary, M.D., F.F.R.*

Fowler, J. F. Oxygen enhancement ratios and depth doses as opposing factors in fast neutron therapy. *Proc. Roy. Soc. Med.*, March, 1965, *58*, 161–162. (From: Postgraduate Medical School, Hammersmith Hospital, London, England.)

Roentgen rays and electrons are less effective in killing anoxic cells than well oxygenated cells by a dose reduction factor of $2.5-3$. However, the dose reduction factor for neutrons is $1.3-1.9$, depending on the neutron energy. The anoxic gain factor for neutrons with a dose reduction factor of 1.6 is $3/1.6 = 1.7$ as defined by Alper. For equal damage to oxygenated cells, neutrons inflict 1.7 times more damage to anoxic cells compared to roentgen rays. Low energy neutrons have poor penetration but good anoxic gain factors, while high energy neutrons have good penetration but lower anoxic gain factors. The depth dose multiplied by the anoxic gain factor gives the anoxic correct depth dose. Neutrons below 5 mev. have poor penetration. Above this energy, neutrons are more effective than roentgen rays in killing anoxic cells. It appears from recent experiments that at 14 mev. the anoxic corrected depth doses may be near the upper limit of the anoxic gain factor. If this is confirmed, there may be little difference between 7 and 14 mev. neutron beams in their advantages for radiotherapy.—*Komanduri K. N. Chary, M.D., F.F.R.*

Morgan, R. L. Fractionation studies with 6 MeV neutrons and 8 MeV x-rays. *Proc. Roy. Soc. Med.*, March, 1965, *58*, 162. (From: M. R. C. Cyclotron Unit, Hammersmith Hospital, London, England.)

Pig skin was irradiated with fractionated doses of 8 mev. roentgen rays and 6 mev. neutrons produced by the M.R.C. 45 inch cyclotron at Hammersmith Hospital. The subsequent reactions were observed from 3 months to 3 years. It has been found that the RBE of fast neutrons increased with the number of fractions into which the dose was delivered. In addition, for similar early reactions, no progressive increase in tissue damage in neutron irradiated areas has been observed up to 3 years. These results seem to provide an explanation for the late tissue damage observed clinically by Robert Stone, who first used neutrons in therapy in the late 1930s. The late effects could be due to an increase in RBE with extended fractionation.

The oxygen enhancement ratio is 1.7 in the case of 6 mev. neutrons compared to 3 in the case of roentgen rays. Hence, anoxic tumors can be treated more effectively. Cartilage which is normally anoxic is liable to more damage and, therefore, neutron therapy of tumors in the vicinity of cartilage is better avoided.—*Komanduri K. N. Chary, M.D., F.F.R.*

CHEN, YUNG FU. Bilateral hemophilic pseudotumors of the calcaneus and cuboid treated by irradiation: case report. *J. Bone & Joint Surg.*, April, 1965, *47A*, 517–521. (From: Surgical Department, Taiwan Provincial Taipei Hospital, Taipei, Taiwan, Republic of China.)

The author presents a case of bilateral pseudotumors of the calcaneus and cuboid in an 11 year old boy with apparent classic hemophilia. The biopsy of the tumor showed a multilocular cystic mass filled with blood. The patient received 1,576 r (tissue dose, mid-plane) in 16 days to the right foot and 1,672 r (tissue dose) in 10 days to the left foot. The factors were: 250 kv., 15 ma., 50 cm. target skin distance and a filter of 2.2 mm. of copper.

The pain subsided 3 days after roentgen therapy was started and completely ceased by the 10th day. Gradually, all the pseudotumors became smaller, and the protuberances had disappeared completely 4 weeks after completion of roentgen therapy. Roentgenograms of the feet, made at this time, showed a decrease in the size of the cysts and what appeared to be some increase in the density of the bone.

The patient has been observed for 2 years and 8 months since treatment, during which time the feet showed no evidence of recurrence of the tumors, and the roentgenographic appearance of the involved bones has improved.

The author states that all the previous reports of the effects of radiotherapy for pseudotumors had been conflicting; the results in this case were dramatic.—*C. Peter Truog, M.D.*

DANESE, CALLISTO, and HOWARD, JOHN M. Postmastectomy lymphedema. *Surg., Gynec. & Obst.*, April, 1965, *120*, 797–802. (From: Department of Surgery, Hahnemann Medical College, Philadelphia, Pa.)

The authors, in a study of the pathogenesis of chronic edema after radical mastectomy, performed lymphangiographic and venographic examinations on 20 patients before and after radical breast surgery. They found three major lymphatic pathways evident in the upper extremity, coursing from the wrist to the antecubital fossa. These consisted of radial, medial, and ulnar routes that paralleled the course of homonymous veins. The epitrochlear lymph nodes were only associated with the ulnar pathway; and efferent channels subsequently reached the axillary lymph nodes via a supra- or subfascial course. The median lymphatics drained directly into the axillary lymph nodes, as did the radial lymphatics. The radial lymphatics may, however, follow the cephalic vein into a deltopectoral lymph node and up into the cervical chain, bypassing the axilla completely. This occurred about 50 per cent of the time in this small series.

In the postmastectomy state in those patients without edema, the contrast medium collected under the skin flap on the anterior chest wall, indicating that postoperative fluid collection in this area consists mostly of lymph drainage. The lymph channels all retained their normal appearance in this group of patients.

In patients with lymphedema, marked dilatation of the lymphatics was present. Dermal backflow and reflux were also evident. In 4 patients with severe and long standing edema, no lymph vessels could be identified at the wrist.

The authors believe that postoperative re-establishment of satisfactory lymphatic drainage is dependent upon the existence of intact lymphatic vessels. That group of lymphatic vessels which accompany the cephalic vein, may, if present and not injured during the operation, provide the necessary collateral flow. If these are absent, some attempt at establishing a collateral flow usually occurs. When a moderate collateral flow ensues, a balanced stage is reached and a stationary phase of the disease results. If the lymphostasis is severe and of long standing, fibroblastic proliferation occurs which produces induration of the edema and probably obliteration of the lymphatic vessels, with a slow progression of the disability. Since venous pressure and venograms were interpreted as normal in all patients, venous obstruction was not considered to play an important rôle in the pathogenesis of this syndrome.

Eleven roentgenographic reproductions and one photograph are included in this paper.—*Kenneth M. Nowicki, M.D.*

GAULT, M. HENRY, and KINSELLA, T. DOUGLAS. Carcinoma of lung with adrenal hyperfunction and hypercalcemia treated by parathyroidectomy. *Canad. M. A. J.*, Feb. 13, 1965, *92*, 317–324. (From: Departments of Medicine and Medical Chemistry, Queen Mary Veterans' Hospital, Montreal, Quebec, Canada.)

The hypercalcemia of malignancy frequently responds to measures such as the administration of adrenocorticosteroids or chelating agents.

The authors report a case of carcinoma of the lung, where the correction of the hypercalcemia was extremely difficult and demonstrate the effects of 2 additional therapeutic measures on the hypercalcemia. The patient presented hypokalemic alkalosis, renal failure, and pancreatitis associated with autopsy evidences of few bone metastases. The probable endocrine-like effect of the tumor on the development of hypercalcemia is postulated.

The 2 additional therapeutic measures employed were: peritoneal dialysis and subtotal parathyroidectomy. The peritoneal dialysis was the most effective of the two, while subtotal parathyroidectomy failed to produce a further decrease in serum calcium values.

The occurrence of hypokalemic alkalosis and the presence of increased adrenocortical function and its relation to the carcinoma of the lung are discussed at length and the possibility is advanced that this neoplasm produces two factors causing systemic effects ordinarily associated with the function of the endocrine glands.

The authors suggest that the hypercalcemia and presumably the adrenal hyperfunction were at least in part due to a humoral factor produced by the tumor.—*Luther W. Brady, M.D.*

RADIOISOTOPES

Bucy, Paul C., and Ciric, Ivan S. Brain scans in diagnosis of brain tumors: scanning with chlormerodrin Hg 203 and chlormerodrin Hg 197. *J.A.M.A.*, Feb. 8, 1965, *191*, 437–443. (Address: Dr. Bucy, 251 East Chicago Avenue, Chicago 11, Ill.)

The authors performed scans, using radioactive mercury compounds (chlormerodrin Hg^{203} and Hg^{197}) for the diagnosis and localization of brain tumors; in 80 cases 105 scans were made. Good localization was obtained in 61 cases; the scan remained entirely normal in 11 cases; and it was termed equivocal in 8 cases.

All of the brain tumors but 1 (probably a metastatic tumor with multiple areas of localized increase in radioisotope concentration) were verified surgically or histologically, or both.

It was found that glioblastomas and meningiomas gave more constant as well as more definite results than other tumors. The technique, however, has not proven sophisticated enough to differentiate types of tumors, nor has it enabled differentiation between neoplasms and granulomas.

Supratentorial tumors led to the greatest number of positive scans. Other tumors which were discovered and localized with scans included sarcomas, intracranial granulomas and metastatic tumors.

Two cases of epidermoid cysts gave negative scans. These tumors are relatively avascular which probably accounts for their failure to pick up the radioactive mercury.

Posterior fossa tumors were not discovered and localized in this series as readily as in others reported in the literature.

The authors feel that the radioactive brain scan has proved to be the most important single procedure for the diagnosis of a brain tumor. It is emphasized that a negative brain scan in a patient in whom neurologic examination and symptoms suggest a tumor should not preclude further investigative studies.—*Ronald Schaupp, M.D.*

Overton, Marvin C., III, Haynie, Thomas P., and Snodgrass, Samuel R. Brain scans in nonneoplastic intracranial lesions: scanning with chlormerodrin Hg 203 and chlormerodrin Hg 197. *J.A.M.A.*, Feb 8, 1965, *191*, 431–436. (Address: Dr. Haynie, Nuclear Medicine Service, University of Texas Medical Center, Galveston, Texas 77551.)

In a 2 year period in 162 patients with complete neurologic diagnostic work-ups including skull roentgenograms, electroencephalograms, cerebral arteriograms, and in some cases, pneumoencephalograms, a final diagnosis of local intracranial disease was made. Of these, 100 had neoplasms and 62 had nonneoplastic lesions. Of the 62 patients with nonneoplastic local lesions, 39 had abnormal scans; 30 were scanned with Hg^{203} (10 μc/kg. to a limit of 700 μc), and 32 with Hg^{197} (in a dose schedule of 700 μc for adults and 500 μc for children).

Accepted scanning procedures were employed after intravenous administration of the Hg compounds. Scans were interpreted by inspection and classified as positive, equivocal or negative. A positive scan showed increased concentration on three passes of the probe over the site of the lesion. An equivocal scan showed lesser degrees of concentration suggestive of abnormality.

Patients with cerebral infarctions formed the largest group of abnormal scans in the series of nonneoplastic lesions. The appearance of the scan in almost all cases of cerebral infarction was that of an area of minimal increase in density and occasionally a wedge or pie-shaped configuration. A correlation between the time of infarction and the results of the brain scans is alluded to. Four out of 5 patients with intracerebral hematomas had positive scans.

Other lesions such as cerebral arteriovenous malformations, cerebral aneurysms, brain abscesses, cerebral contusions, subdural hematomas and abscesses all proved to have a relatively high percentage of positive results on brain scans. Only 1 false positive case was encountered. A rather unusual positive brain scan was found in a patient with acute multiple sclerosis.

The reason for concentration of radioactive materials in nonneoplastic as well as neoplastic intracranial lesions is not precisely known. Abnormal accumulation of a wide variety of radioactive substances has been attributed to a presumed alteration in the blood brain barrier.

The findings reported in this paper as well as other published reports emphasize the point that when utilizing the brain scan as a diagnostic method to detect and localize intracranial neoplasms, abnormal scans will be found in a number of patients with nonneoplastic disease. These positive scans must be carefully evaluated before assuming that the positive area does or does not represent a neoplasm or space-occupying lesion.—*Ronald Schaupp, M.D.*

Witcofski, Richard, Maynard, Douglas, and Meschan, I. The utilization of ^{99m}technetium in brain scanning. *J. Nuclear Med.*, Feb., 1965, *6*, 121–130. (From: Department of Radiology, The Bowman Gray School of Medicine, Winston-Salem, N. C.)

The most widely used agents for brain scanning at the present time are the mercurial diuretics, Hg^{203} and Hg^{197} chlormerodrin. Hg^{203} chlormerodrin gives a higher renal dose (40–70 rads/mc) than the Hg^{197} compound. The energy of the Hg^{197} is 77 kev. and is not ideal for brain scanning.

The Tc^{99m} is obtained from a Mo^{99}-Tc generator. The parent, Mo^{99}, decays with a half life of 67 hours to produce a short lived daughter product, Tc^{99m} (half life of 6 hours). Tc^{99m} decays to Tc^{99} with a gamma emission of approximately 140 kev.

A dose of 10 μc of Tc^{99m} is given orally in an isotonic saline solution with the patient being in a fasting state. The patients are instructed to move about or to lie on their right side to speed up gastric emptying. Scanning is begun after 30–45 minutes with the window set at 130–160 kev., a scan speed of 50–60 cm. per minute and a line spacing of 0.25 cm. Both lateral scans are routinely done with either an anterior or posterior scan, depending on the findings on the lateral scans and the clinical impressions.

A series of 142 patients was scanned, using Tc^{99m}, and there were 24 abnormal scans; 12 of the abnormal scans were verified by pathologic diagnoses, 7 vascular abnormalities were verified by arteriography, and the other 5 correlated well with the clinical impressions. There were 3 proven false negatives: pituitary tumor, lipoma of the corpus callosum, and cerebellar metastases from a lung adenocarcinoma.

The following cases were adequately visualized using Tc^{99m}: 6 malignant gliomas, 2 meningiomas, 4 arteriovenous malformations, 2 cerebellar metastases, 1 brain abscess, 1 acoustic neuroma, and 3 cerebral infarcts.

The advantages of using Tc^{99m} for brain scanning are: it can be given orally; an optimum scanning energy of 140 kev.; high count rate with a lower patient radiation dose; scanning can begin within one-half hour after an oral dose; and adequate delineation and visualization of brain lesions.

The disadvantages are: the Tc^{99m} must be obtained from the generator daily; rapid decay of Tc^{99m} does not permit shelf storing; the patient must be fasting; possible extracranial contamination from saliva-producing artifacts; and the Tc^{99m} is not always absorbed in an adequate amount.

The authors were able to obtain more technically satisfactory scans using Tc^{99m} than Hg^{197} in the dosage range normally used.—*Charles W. Cooley, M.D.*

McAfee, J. G., Stern, H. S., Fueger, G. F., Baggish, M. S., Holzman, G. B., and Zolle, L. ^{99m}Tc labeled serum albumin for scintillation scanning of the placenta. *J. Nuclear Med.*, Dec., 1964, *5*, 936–946. (From: Departments of Radiological Science, Obstetrics and Gynecology, Johns Hopkins University Schools of Medicine, Hygiene and Public Health, Baltimore, Md.)

The authors review the history of attempts to localize the placenta with radioisotopes, and then describe the preparation of Tc^{99m} human serum albumin. The value of this tracer isotope in reducing patient radiation exposure is now well known. A number of scans performed with "Technetated" HSA are shown, and they afford excellent visualization of the structure of the placenta.

Tissue distribution of Tc^{99m} serum albumin is then reviewed, and the expected considerable reduction of patient dose to both mother and fetus and to maternal and fetal thyroid glands is described, based in part on theoretic calculations. The method seems well worth investigation.—*Frederick J. Bonte, M.D.*

Meckelnburg, R. L. Clinical value of generator produced 87-M strontium. *J. Nuclear Med.*, Dec., 1964, *5*, 929–935. (Address: Department of Isotopes and Endocrinology, Memorial Hospital, Wilmington, Del.)

Bone scanning with strontium 85 is a recognized clinical technique practiced in many radioisotope laboratories. The isotope strontium 87m also has some rather attractive features for this purpose. Its half-life of 2.8 hours and the absence of any beta emission assure reduced patient radiation exposure, while the .388 mev. gamma ray is an easy one to measure with existing commercial apparatus.

The author describes a system consisting of a column which contains the parent, yttrium 87, which is itself produced by cyclotron bombardment of strontium 87. The half-life of the parent yttrium 87 is 80 hours, and it is kept in place by adsorption onto BioRad AG-1, X-8 resin in an ion exchange column. Thereafter the generator may be eluted with ammonium carbonate, and after the initial stabilization phase the percentage of the parent present in the eluate is negligible. Per 100 μc dose of strontium 87m, the dose to the bone is estimated at 40.5 mrads and the dose to the whole body at 1.2 mrads, as opposed to figures of 3.7 rads and 1.1 rads, respectively, were a dose of 100 μc of strontium 85 to be used. Several scans made with strontium 85 are presented and are of the usual quality of radiostrontium bone scans.

The generator method of production of strontium 87m seems to have much to recommend it to any laboratory heavily engaged in bone scanning with radiostrontium.—*Frederick J. Bonte, M.D.*

Pozananski, Thomas W., and Frankel, Sam. The roentgenographic development of radiostrontium (Sr^{90})-induced osteogenic sarcoma in the rat. *J. Bone & Joint Surg.*, March, 1965, *47A*, 349–358. (Address: 216 South Kingshighway, St. Louis, Mo.)

In a control study 60 rats were injected with a single known cancerogenic intraperitoneal dose of 0.75 microcurie of Sr^{90} per gram of body weight. Roentgenograms of the injected and controlled animals were obtained at 14 day intervals, or more frequently when clinically indicated, with the animals anesthetized for the procedure. At the death of the animal, terminal roentgenograms were also made, and a complete postmortem examination was performed.

Osteogenic sarcoma developed in 39 of the injected rats (65 per cent). A combined percentage of 58.8 per cent of the neoplasms occurred in the spinal column, followed by 28 per cent in the long bones. In addition to the primary site neoplasm, 18 of the 39 rats (46.1 per cent) exhibited a total of 29 separately arising osteogenic sarcomata. Pulmonary and lymphatic metastases were present in 64.5 per cent.

The earliest time that an osteogenic sarcoma was visualized roentgenographically was 150 days after injection of Sr^{90}; the latest, 206 days. There was a tendency for tumors to be predominantly either boneforming, or non-boneforming, with completely osteolytic tumors being rare. In tumors of long duration, a tremendous amount of newbone formation was common, and a large soft-tissue mass, often containing flecks of neoplastic bone, was present contiguous to the bone.

Sr^{90} is a known bone seeker, which is concentrated rapidly at sites of active bone growth within 1 to 2 hours after injection. The most recent work indicates that the mechanism of strontium turnover is apparently an ion exchange at the surface of the bone mineral with no indication of intracrystalline incorporation. Radiation damage to the bone is the result of the long physical half-life of 27.7 years and the high beta energy produced. Reportedly, the maximum penetration of Sr^{90}$-$Y^{90} beta particles through bone is approximately 5.5 mm. with an average range of 1.3 mm.

It is known that an osteogenic sarcoma can be induced in man by internally deposited radium and following injury to bone from external radiation. Radiostrontium constitutes a relatively large fraction of the fission products produced in a nuclear explosion, but to date, no instances of Sr^{90}-induced osteosarcoma have been reported in man.—*Donald M. Monson, M.D.*

Rose, G. Alan, Reed, G. W., and Smith, A. H. Isotopic method for measurement of calcium absorption from the gastro-intestinal tract. *Brit. M. J.*, March 13, 1965, *1*, 690–692. (From: University Departments of Medicine, and Medical Physics, the General Infirmary at Leeds, England.)

The authors used a combination of the Ca^{47} test with the conventional calcium balance test to study the calcium absorption from, and secretion into, the bowel. Twenty-three of the 25 patients studied had various disorders of calcium metabolism.

A dose of 10 μc Ca^{47} was given either in one dose or distributed during the day with the meals. The single dose method gave a better correlation between true and net calcium absorption. The stools were left in the original cartons and the radioactivity was measured in a cylindrical array of Geiger-Mueller counters. The counter geometry gave a uniform sensitivity of response over a volume large enough to include the carton. The sample were measured in a lead container with a wall of 2 mm. thickness to screen out the radiation from Sc^{47} to which the calcium isotope decays. The stools were checked until no radioactivity was detected. The percentage of isotope absorption was determined. The true calcium absorption, the net calcium absorption and the net secreted calcium were determined. The true calcium absorption is a product of the percentage isotopic absorption and the dietary calcium. The net calcium absorption is the difference between the dietary calcium and the fecal calcium obtained during the same metabolic period. The net secreted calcium is obtained by subtracting the net calcium absorption from the true calcium absorption.

The secreted calcium was not raised in metabolic conditions most commonly associated with raised fecal calcium. The cause of the high fecal calcium was, in all cases except one, due to failure to absorb calcium and not to a rise in calcium secretion in the gastrointestinal tract. It is believed that most of the calcium secretion is in the bile and succus entericus. The net secreted calcium is virtually the true secreted calcium. The net secreted calcium was reasonably constant in most patients studied, but exceptions did occur.

The present series of radioisotopic tests for calcium absorption gave constant and reliable results. It was concluded that the oral Ca^{47} test could be used as an alternate to the conventional calcium balance studies as a means of finding net calcium absorption.

The advantage of using the Ca^{47} test is that there is no need for handling or chemical studies of the stools.—*Charles W. Cooley, M.D.*

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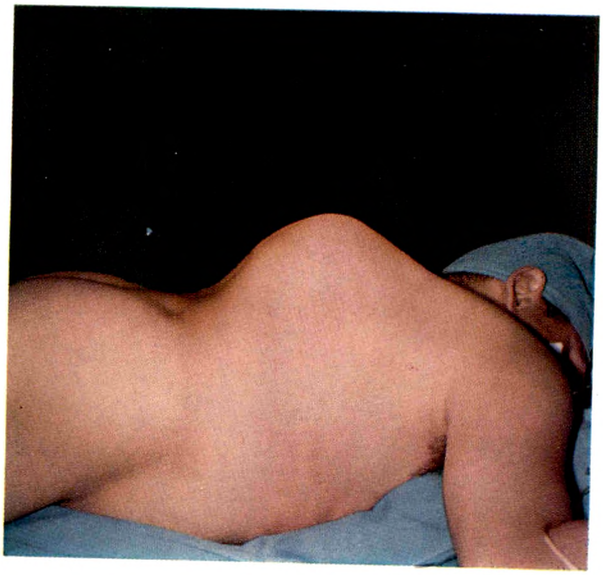

TUBERCULOSIS OF VERTEBRAL COLUMN

(Pott's Disease)

Kyphosis of vertebral column due to tuberculosis

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Neurological study showed weakness of calf muscles and left posterior thigh muscles. Also noted were bilateral, hyperactive, deep-tendon reflexes with spasticity. Babinski's sign was positive bilaterally with bilateral ankle clonus. Skin sensation was decreased between levels of T11 and S3.

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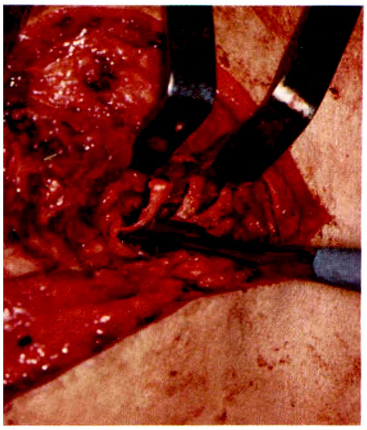

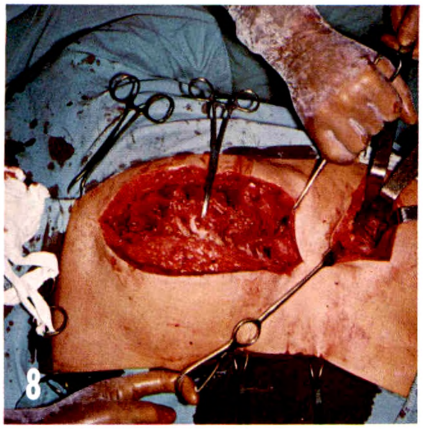

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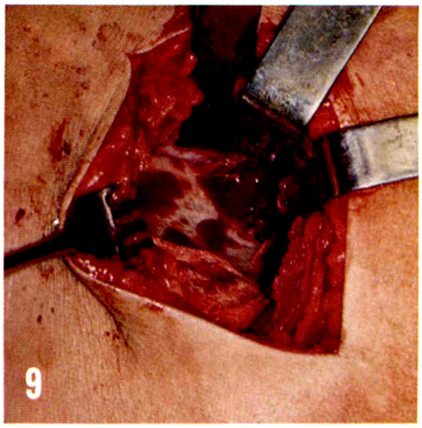

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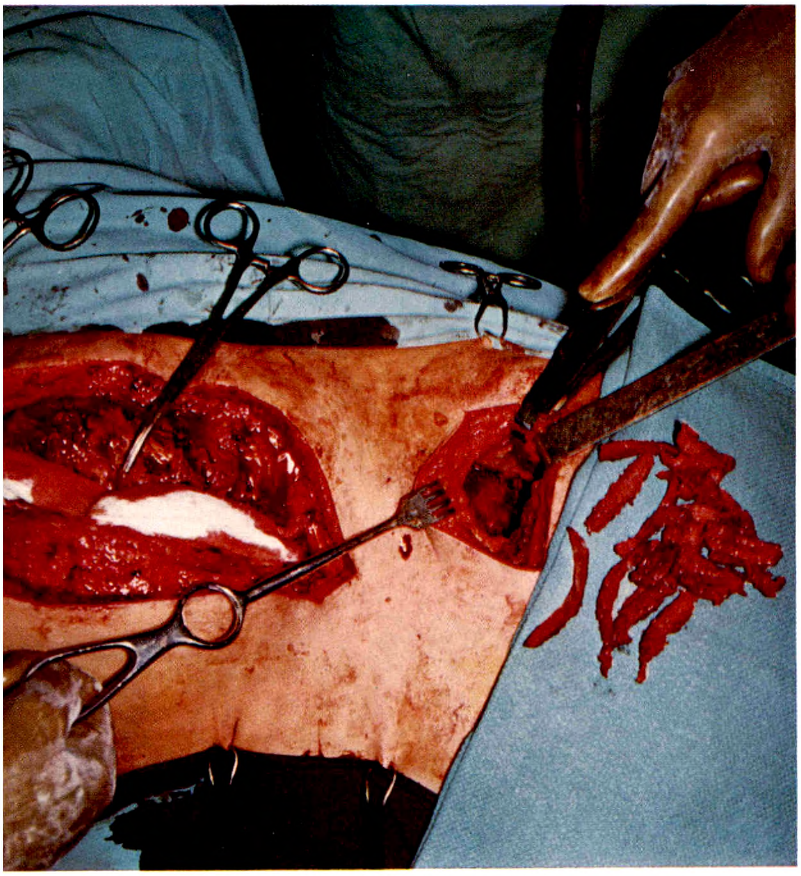

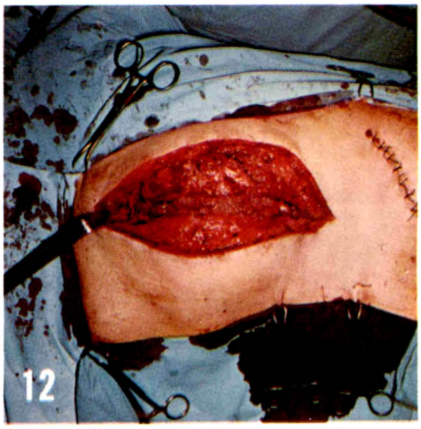

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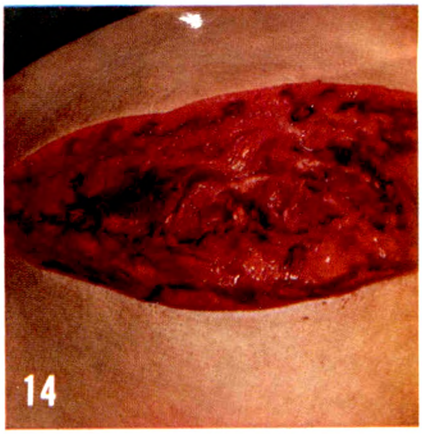

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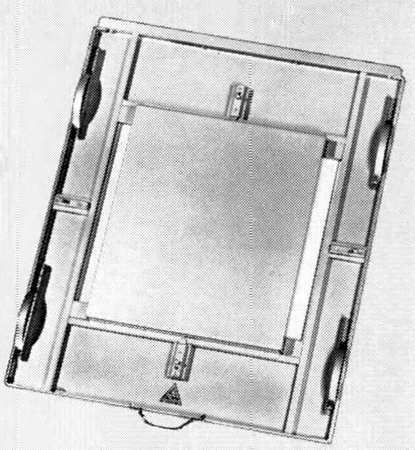

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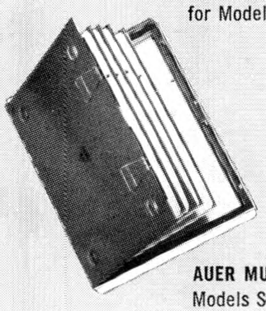

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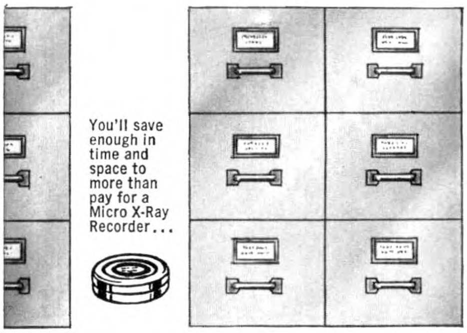
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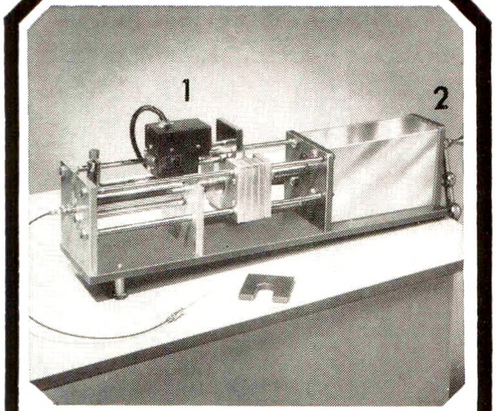

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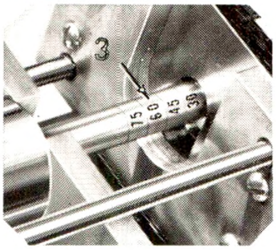

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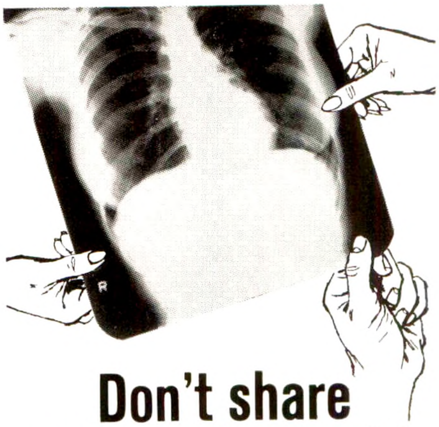

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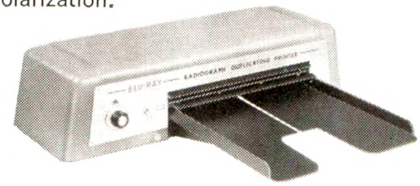

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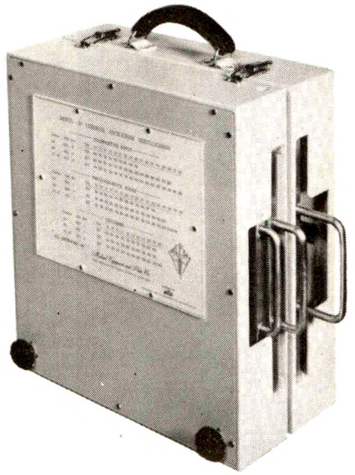

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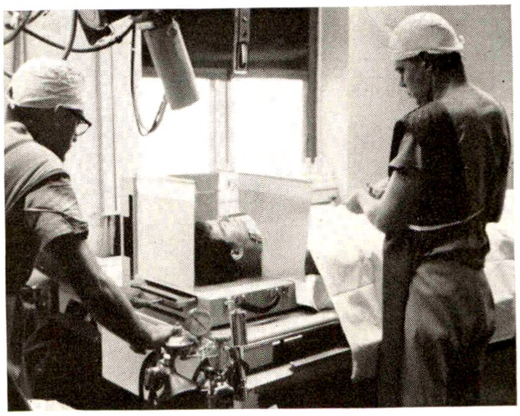

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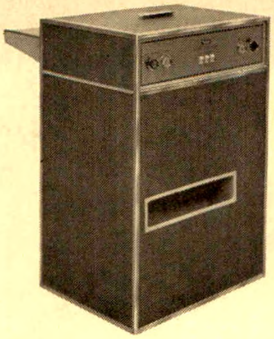

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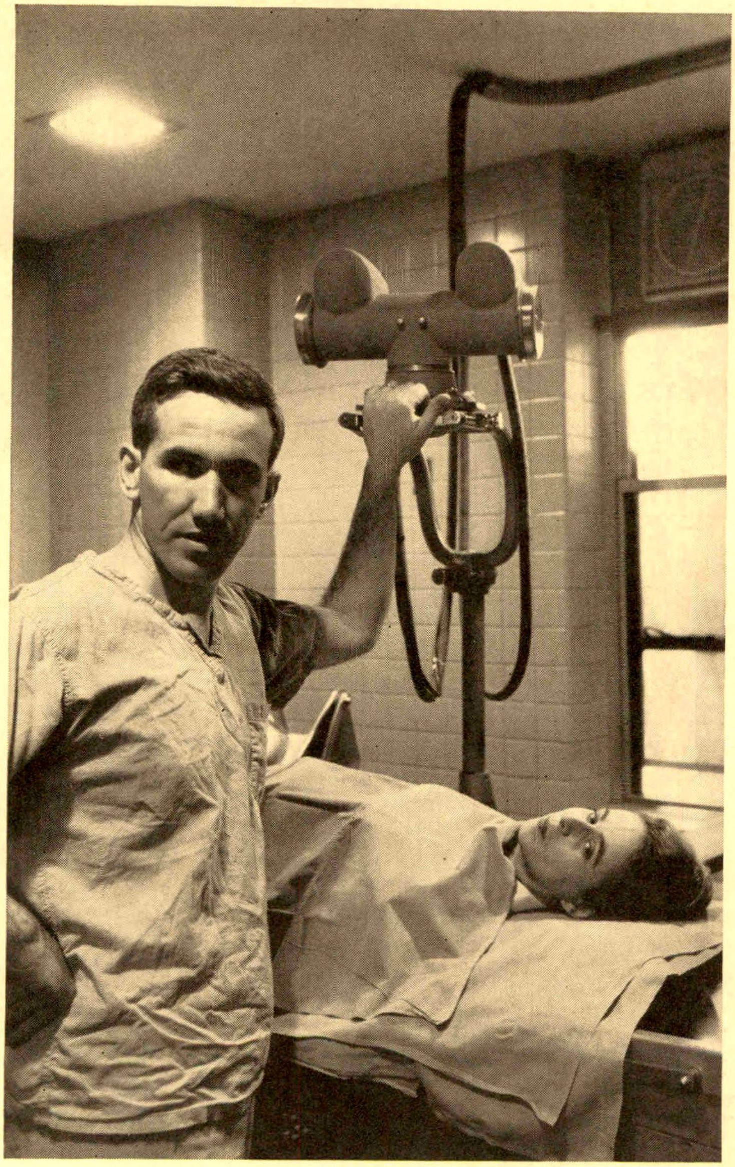

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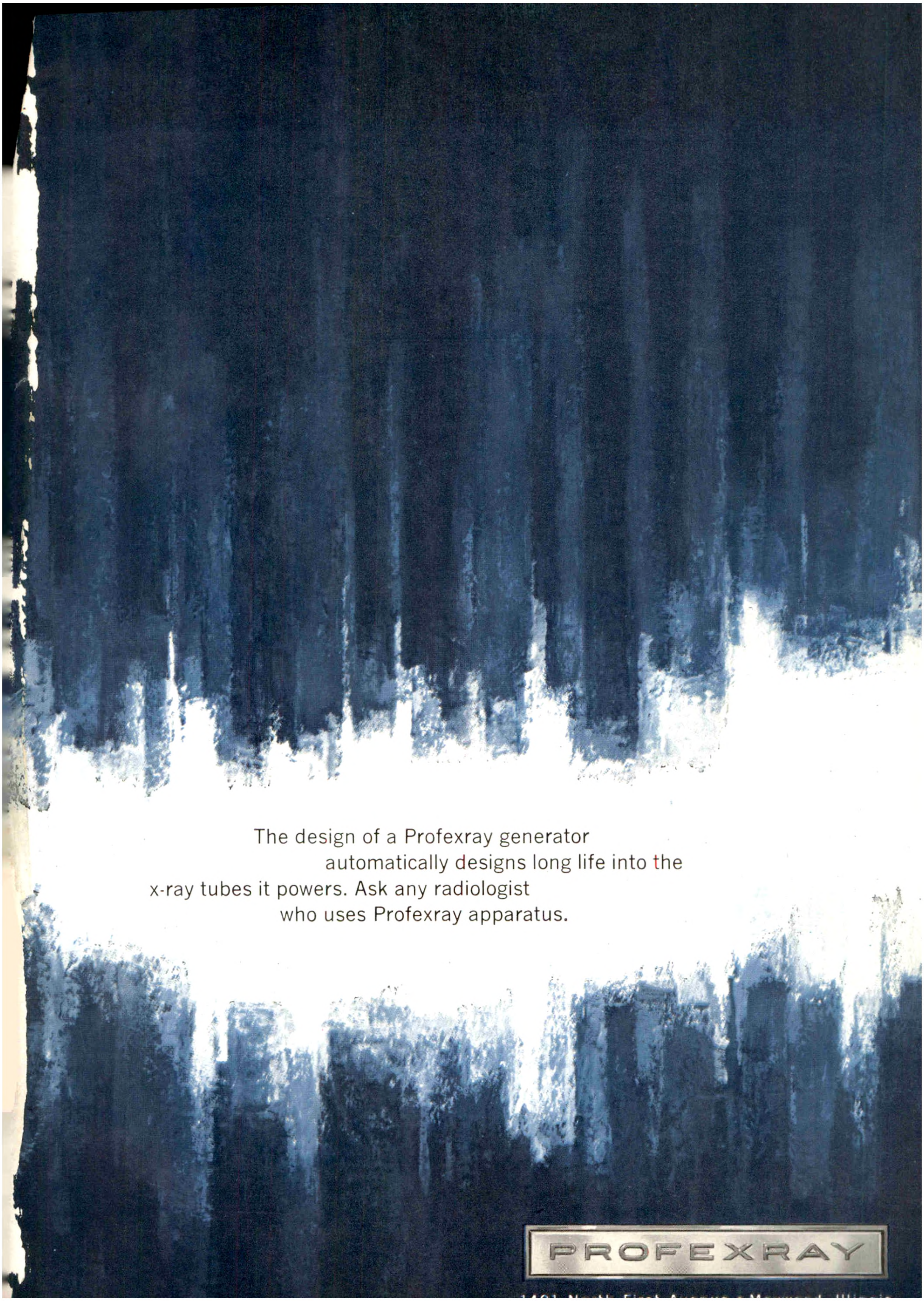

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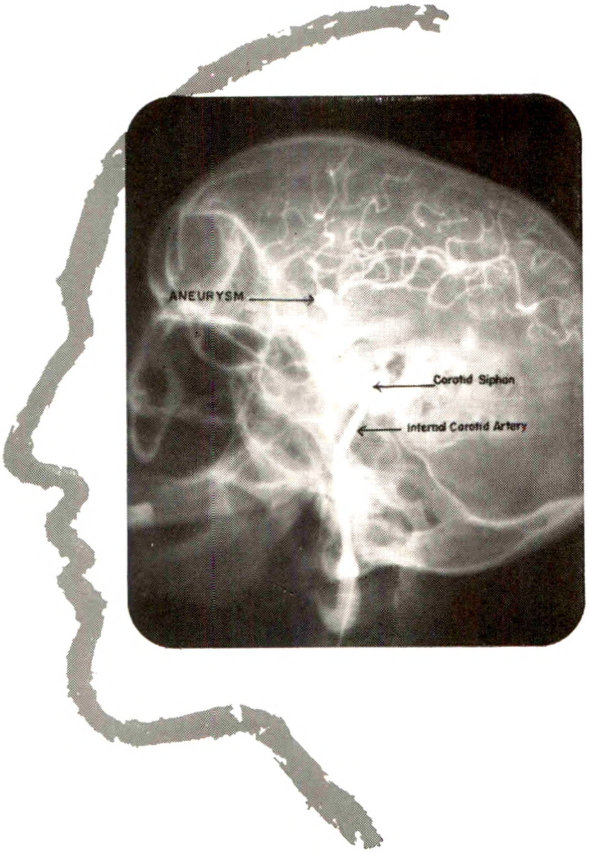

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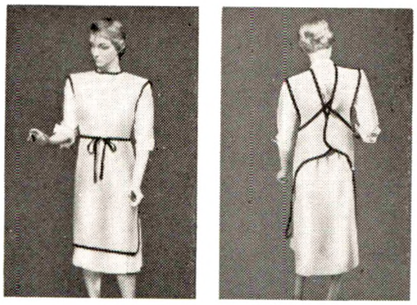

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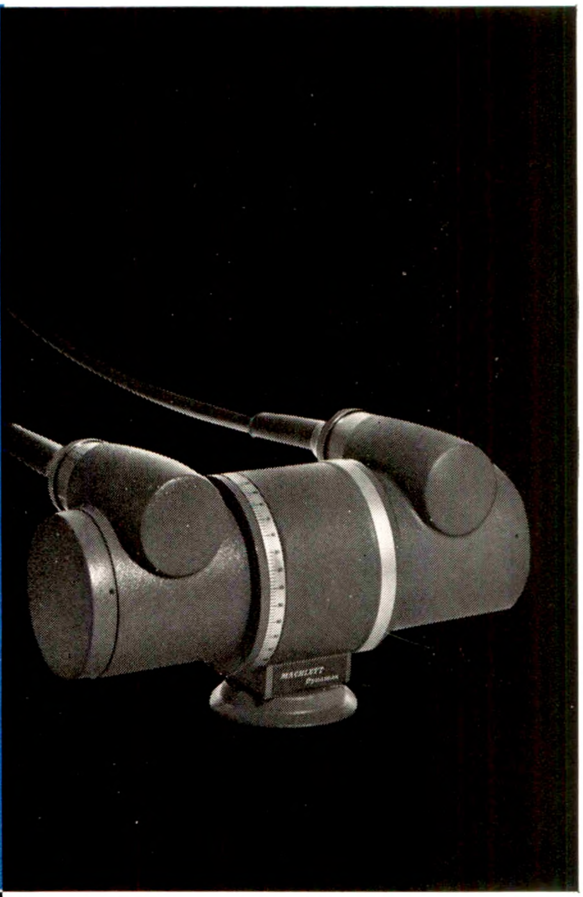

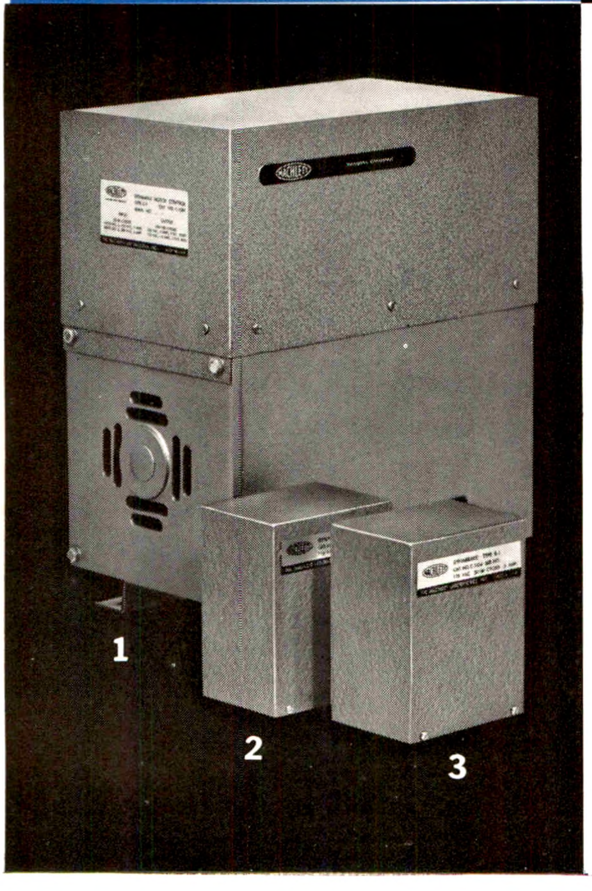

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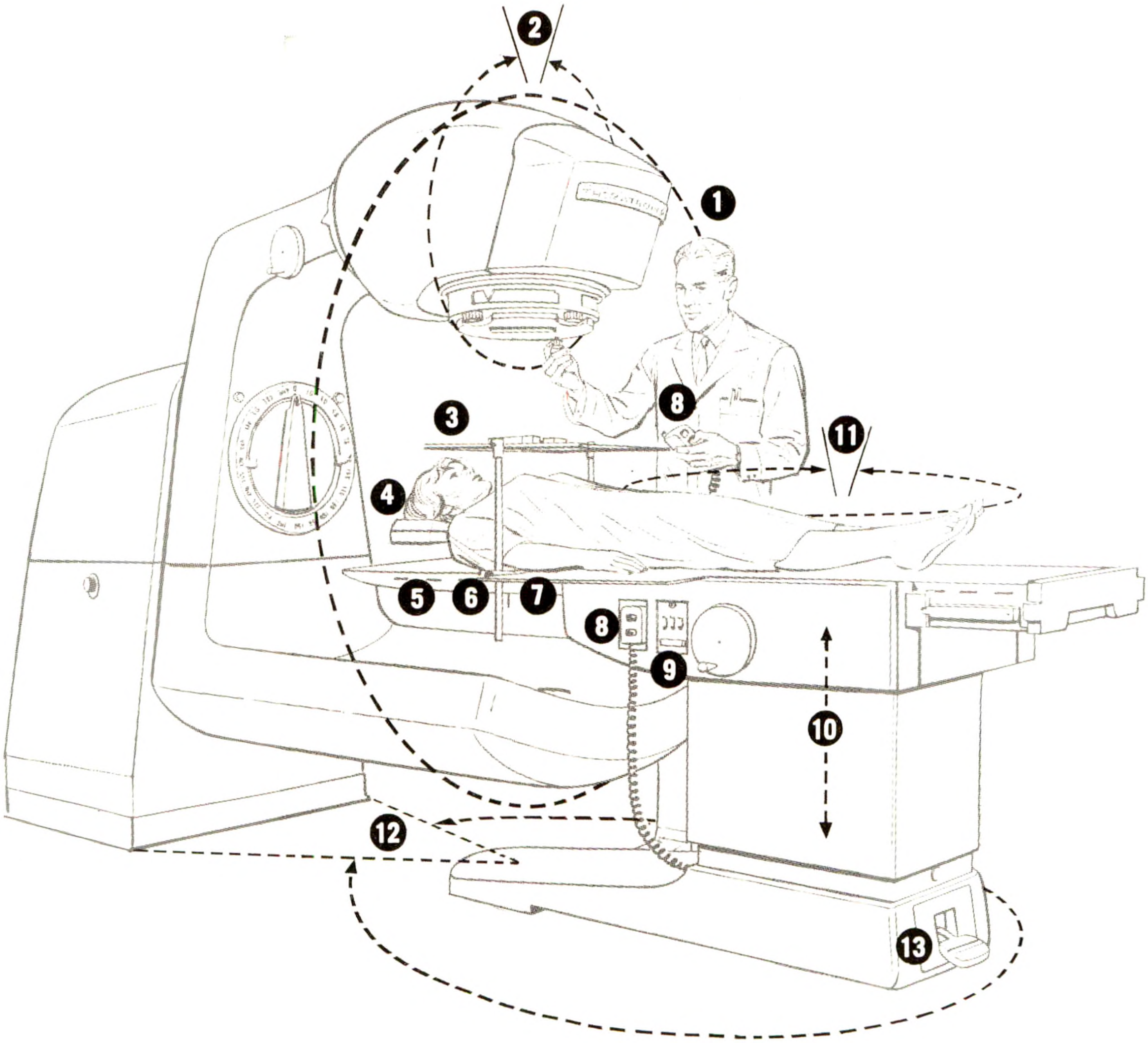

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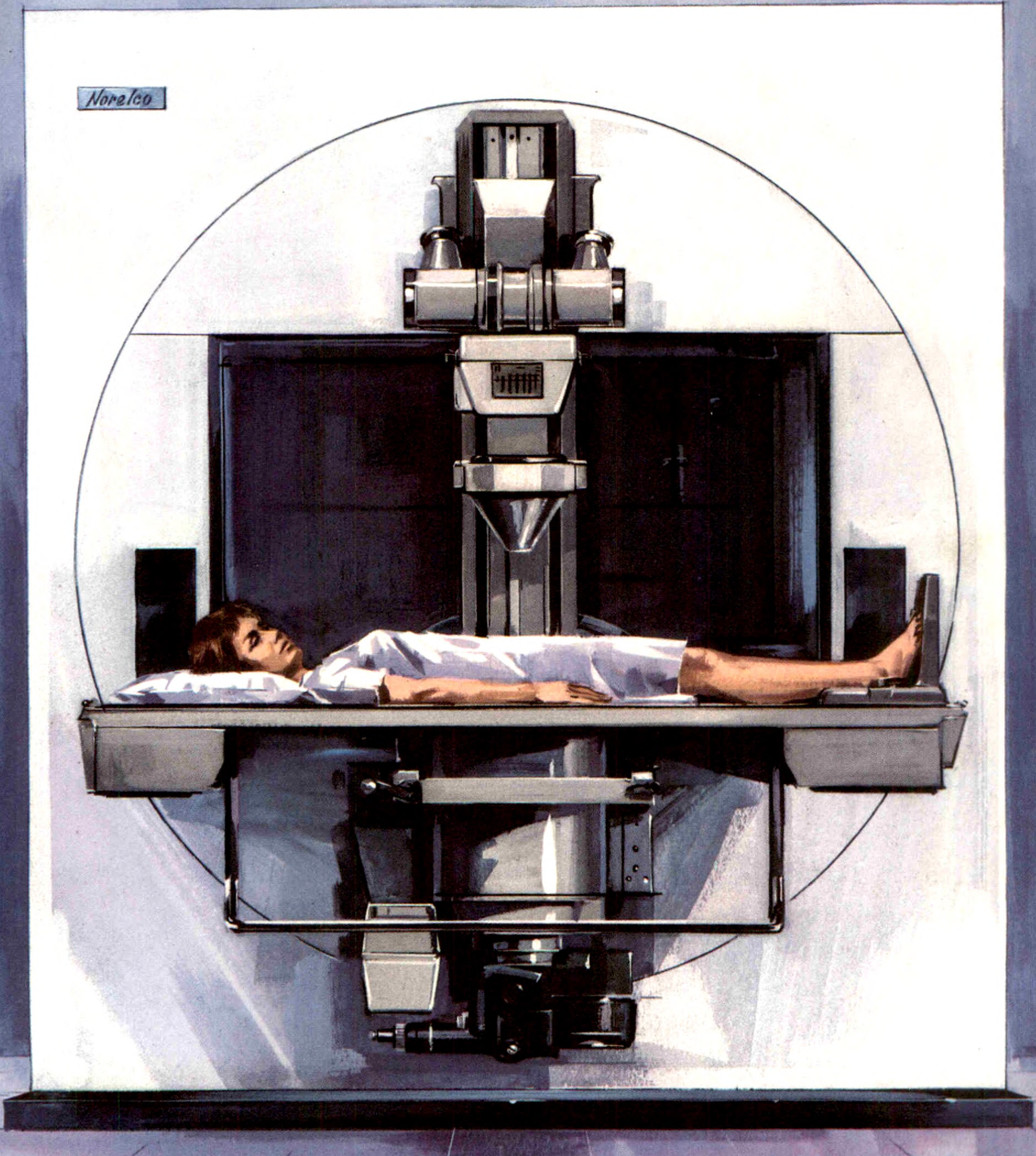

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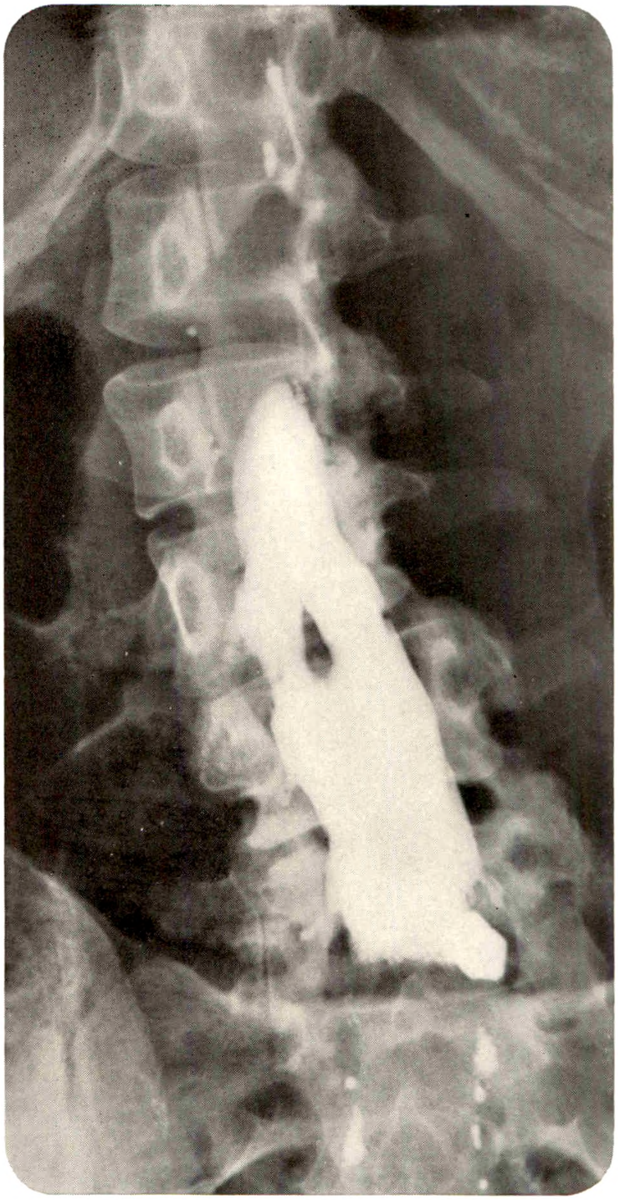

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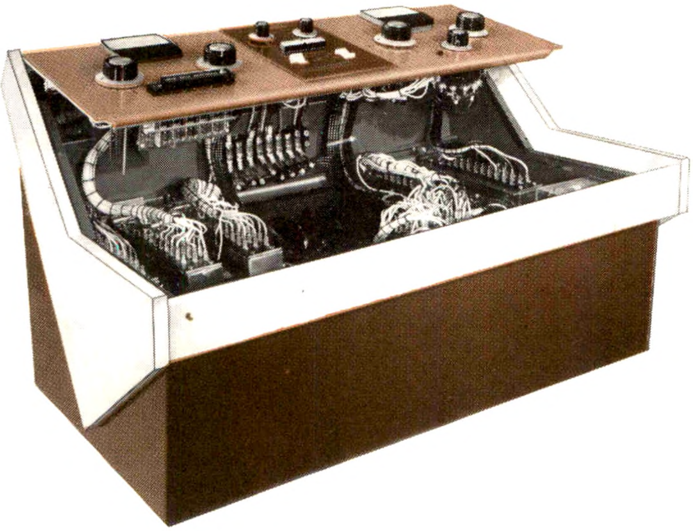

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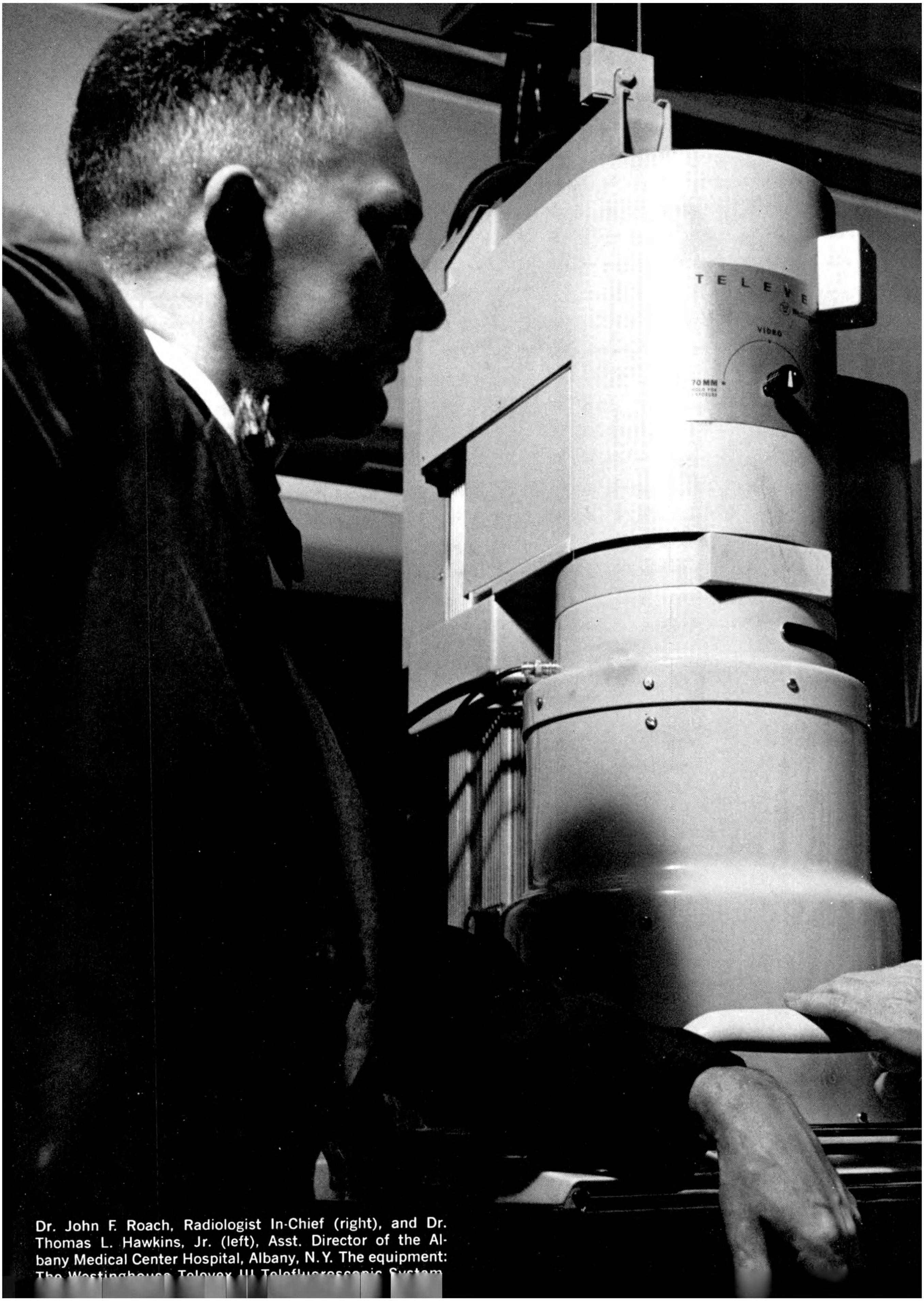
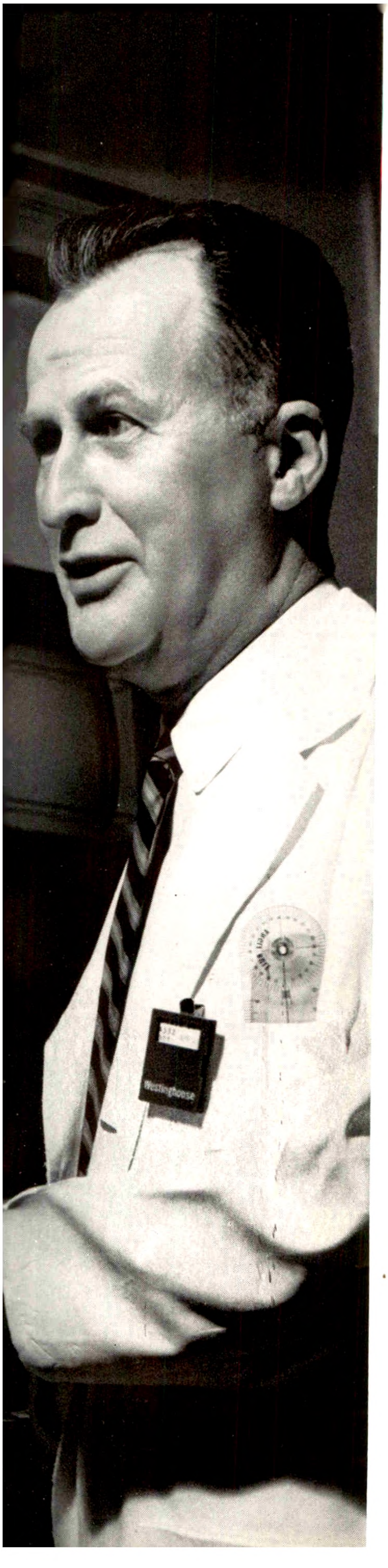


Dr. John F. Roach, Radiologist In-Chief (right), and Dr. Thomas L. Hawkins, Jr. (left), Asst. Director of the Albany Medical Center Hospital, Albany, N.Y. The equipment: The Westinghouse Televex III Telefluoroscopic System.



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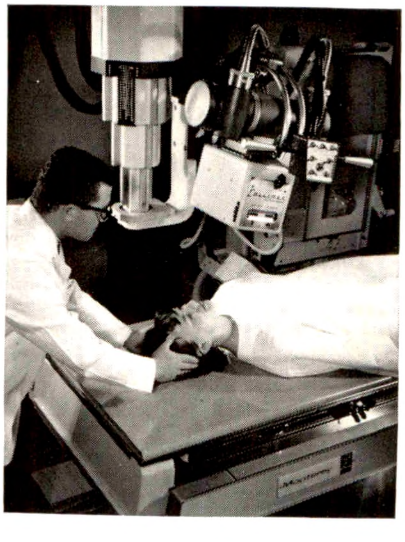

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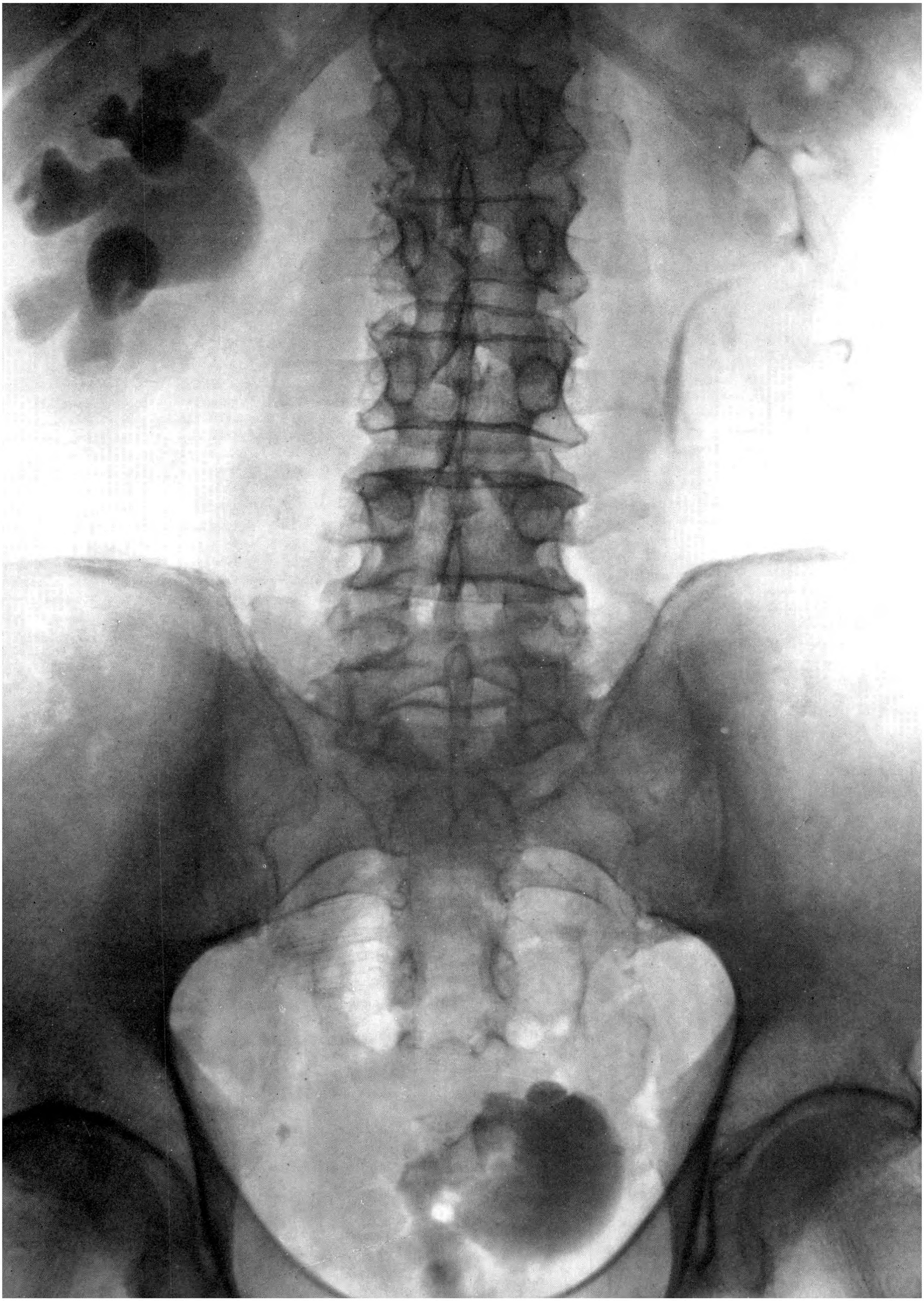

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RADIUM THERAPY AND NUCLEAR MEDICINE

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DRIP INFUSION PYELOGRAPHY*

By ARTHUR J. WENDTH, JR., M.D.†
ALBANY, NEW YORK

DURING recent years an increasing number of reports have appeared in the medical literature in which the use of large amounts of contrast material in order to obtain diagnostic visualization of the renal parenchyma and collecting systems is advocated.[2,3,6,7,9,10] Perhaps the most significant of these is the report by Schencker[6] who, for the first time, used massive doses of contrast material and showed not only that this was a safe and efficient method for obtaining clear demonstration of the collecting systems, but also that the method provides nephrograms of a quality permitting accurate differentiation between renal cysts and tumors.

In the past, relatively few nephrotomographic procedures have been performed in our department, and in these the Evans technique was utilized.[2] Although the results were rewarding in differentiating renal cysts from tumors, we found this type of study somewhat cumbersome. Moreover, the procedure was fraught with inherent pitfalls and presented a certain "chance factor" of exposing the arterial phase film precisely at the proper instant as determined by the arm to tongue decholin circulation time. Also, the need for special equipment was a disadvantage although not an insurmountable one. The greatest problem, however, was the necessity for maintaining coordinated teamwork throughout the entire procedure, in order to obtain properly timed and exposed films, despite the fact that the study was only occasionally performed. It becomes immediately obvious then, that such a study required considerable special planning and scheduling.

Through personal communication, word was received of the work being performed by Schencker and his associates with drip infusion pyelography (DIP) and drip infusion nephrotomography (DIN), and we proceeded to evaluate the techniques for these procedures at this hospital. The present study originated in the fall of 1963 when our first DIN examination was performed. In this procedure we used 1 ml. of contrast material per pound of body weight diluted with an equal volume of 5 per cent glucose in water.

From this initial venture, we began our own investigation. It is interesting to note that, without further communication with the Schencker group, we arrived at some of the same conclusions included in their original paper. Some additional indications and areas of utilization were established in our own study and these will be elucidated below.

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METHOD

The patient is prepared for examination by the administration of 2 ounces of castor oil the preceding afternoon. We do not give a cleansing enema since it causes an increase in the residual gas within the lower alimentary tract. The patient is given his normal evening meal and thereafter is allowed a diet that includes gelatins, puddings, and warm semi-solid cereals. Moreover, he is actually encouraged to keep himself fully hydrated until such time as the procedure is performed. This latter practice serves a twofold purpose: (1) by hydrating the patient, we have maintained an adequate renal arterial blood flow, thereby enhancing the glomerular filtration of the contrast agent, and (2) we are able to perform the procedure in a patient who is usually relaxed, free of hunger and thirst, and relatively comfortable, no matter what time of day the study is performed.

Methylglucamine diatrizoate 60 per cent (renografin 60*), our current agent of choice, is mixed in equal volumes with 5 per cent glucose in water for administration to the patient according to the following dosage schedule:

Body Weight of Patient	Dosage of Contrast Agent
Less than 60 lb.	1 ml. of contrast agent per lb. of body weight plus an equal volume of diluent
60–120 lb.	125–150 ml. of contrast agent plus an equal volume of diluent
120–200 lb.	200 ml. of contrast agent plus an equal volume of diluent
over 200 lb.	250 ml. of contrast agent plus an equal volume of diluent

The bottle containing both contrast material and diluent is suspended from a fully extended intravenous pole so that it is approximately 8 feet above the floor and about 4 feet above the level of the patient. The solution is then allowed to run as fast as possible into an antecubital or femoral vein of the patient by means of a needle with as large a bore as possible. Usually a 16 or 18 gauge Rochester needle is adequate in adults. The total time of infusion in our series has ranged between 2½ and 8 minutes with the average time of administration being 5 minutes and 12 seconds.†

For DIN studies, films are exposed at preselected levels following the completed infusion. Of importance here is the fact that the contrast agent remains in the renal collecting system in sufficient concentration to obtain good tomograms for several hours after infusion; hence, serial studies of different sections can be obtained at a leisurely pace. Following tomography, an ordinary roentgenogram of the abdomen is made and this, in turn, is followed by a second roentgenogram, 30 minutes later.

If a DIP study is to be carried out without tomography, films are routinely exposed following the introduction of approximately one-half of the total dose of contrast agent, and films are exposed again at the completion of the infusion. Three films are then exposed at intervals of 5 minutes each. Finally a 30 minute roentgenogram is taken. Thereafter, further roentgenograms are made as deemed necessary in the individual case.

PRESENT STUDY AND INDICATION FOR USAGE

At the time of this writing, a total of 110 examinations have been performed using the infusion technique described above.

Of this total number, 26 were DIN studies to differentiate cysts from tumors, 61 were DIN examinations for better definition of findings noted on previous intravenous pyelograms or in the DIP examinations then in progress, and 23 were DIP procedures for the evaluation of collecting systems and/or parenchymal structures that had failed to visualize at all or had visualized only poorly in previously obtained intravenous pyelograms.

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* Renografin is a trade name of E. R. Squibb & Sons, New York, New York.

† One case was deliberately infused over a period of 15 minutes because of a suspected marginal cardiac decompensation as noted below; this case is not included in these figures.

The impetus to explore the possibility of the infusion technique in the case of a previously nonvisualized kidney came early in our series because of the obviously improved visualization of all parts of the collecting system on the DIN films. After this initial success, we departed more and more from a conservative attitude and soon were performing this type of study in cases of both acute and chronic renal disease. In time, it naturally evolved that an elevated blood urea nitrogen and/or serum creatinine became one of the chief indications for the drip infusion technique.

Up to the present, the infusion technique has been used in either DIP or DIN examinations in order to study the following diseases or clinical symptomatology:

A. Infections and Related Problems
  1. Idiopathic pyuria
  2. Medullary sponge kidney
  3. Calcareous pyelonephritis
  4. Chronic pyelonephritis
  5. Acute pyelonephritis
  6. Chronic glomerulonephritis
  7. Subacute glomerulonephritis with superimposed acute exacerbation
  8. Renal tuberculosis

B. Neoplastic and Cystic Disease
  1. Renal carcinoma
  2. Renal cysts—single and multiple
  3. Polycystic disease

C. Mechanical
  1. Acute obstruction secondary to ureteral stone
  2. Ureteral obstruction secondary to retroperitoneal disease, in cancer of cervix, and other conditions —combined frequently with lymphangiography
  3. Autonephrectomy secondary to prolonged complete ureteral obstruction
  4. Hydronephrosis in an obstructive polycystic kidney

D. Miscellaneous Disease Entities and Signs or Symptoms
  1. Idiopathic hematuria
  2. Diabetic nephropathy
  3. Tubular necrosis
  4. Pheochromocytoma (for adrenal visualization)*
  5. Costovertebral angle pain
  6. Hypertension
  7. Unexplained azotemia
  8. Persistent fetal lobulation
  9. Horseshoe kidney
  10. Agenesis of one kidney
  11. Retroperitoneal fibrosis

Up to this time, the youngest patient examined by either technique was 8 months of age and the oldest was 88 years of age.

The following cases are representative of those in which DIP and DIN examinations have been carried out in our department.

REPORT OF CASES

Case I. E.McL., a 70 year old white female, entered this hospital for diagnostic studies because of right upper quadrant abdominal pain of 2 months' duration. The findings of a series of studies of the gastrointestinal tract, of a barium enema examination and a cholecystographic series were all normal. Intravenous pyelography revealed a possible mass in the right upper pole but the right and left kidneys were otherwise normal. Blood pressure, blood urea nitrogen and serum creatinine were all normal. A DIN examination was performed. It revealed a renal cyst in the right upper pole, 6×7 cm. in size, and an unsuspected cyst in the left lower pole, 2.5×5.0 cm. in size. Impression: Bilateral renal cysts (Fig. 1).

Case II. E.B., a white female 67 years of age, was transferred to this hospital because of gross hematuria associated with urinary frequency and urgency of 10 days' duration. Intravenous pyelography, carried out at another hospital, demonstrated what appeared to be a large mass in the left upper pole which was distorting the collecting system on that side. Blood urea nitrogen, serum creatinine and blood pressure values

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* It has been noted that the liver, spleen and occasionally the adrenals become opacified due to the contrast agent contained in them.

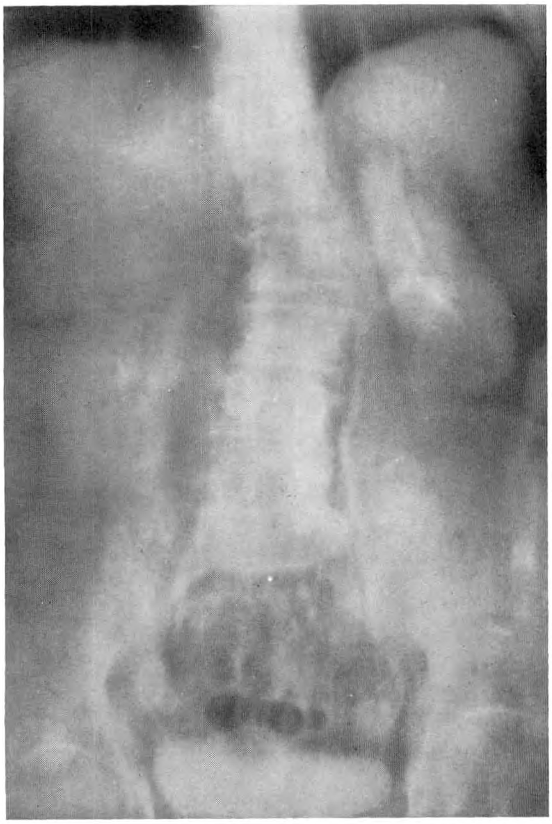


FIG. 1. Case I. Drip infusion pyelogram showing a renal cyst in the right upper pole and one in the left lower pole.

were all normal. A DIN study was performed. This demonstrated a solid mass, 8×6 cm. in size, occupying the entire left upper pole and obstructing the collecting system in this area so that only splayed lower pole calyces were seen (Fig. 2). Impression: Solid tumor, *i.e.*, carcinoma of the left upper pole. This diagnosis was subsequently verified at nephrectomy.

CASE III. H.V.S., a white female 59 years old, had a hysterectomy in September, 1963, for carcinoma of the endometrium. In mid-1964 the patient developed low back pain but delayed a follow-up visit for 3 months. She was readmitted with acute urinary retention in late September. Pelvic examination at that time revealed an obvious vaginal recurrence of carcinoma with a palpable pelvic mass on the right side and a suspected "fullness" high on the left side. Blood urea nitrogen, serum creatinine and blood pressure values were all normal. Bilateral lymphangiography of the lower extremities was performed. This revealed an area of nonfilling in the left iliac chain which was thought to represent complete replacement of several lymph nodes by metastatic carcinoma. Drip infusion pyelography (Fig. 3) confirmed the presence of a mass on both sides of the pelvis and revealed that the one on the right had obstructed the ureter, whereas that on the left had not yet affected the ureteral lumen. Bilateral bladder defects were also seen as a result of these

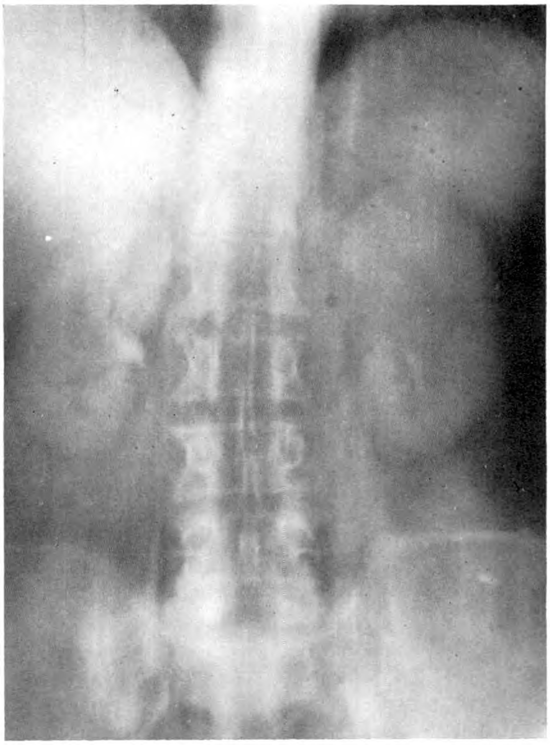
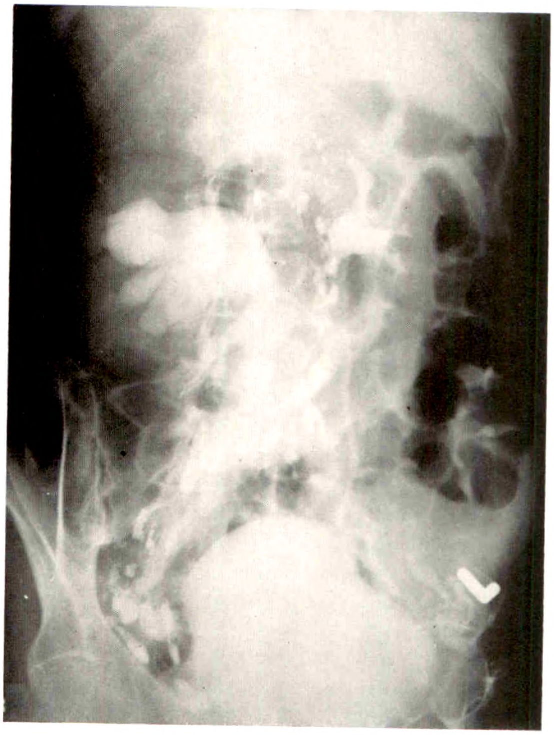


FIG. 2. Case II. Drip infusion nephrotomogram showing a solid mass occupying the entire upper pole of the left kidney and obstructing the collecting system.

»»→

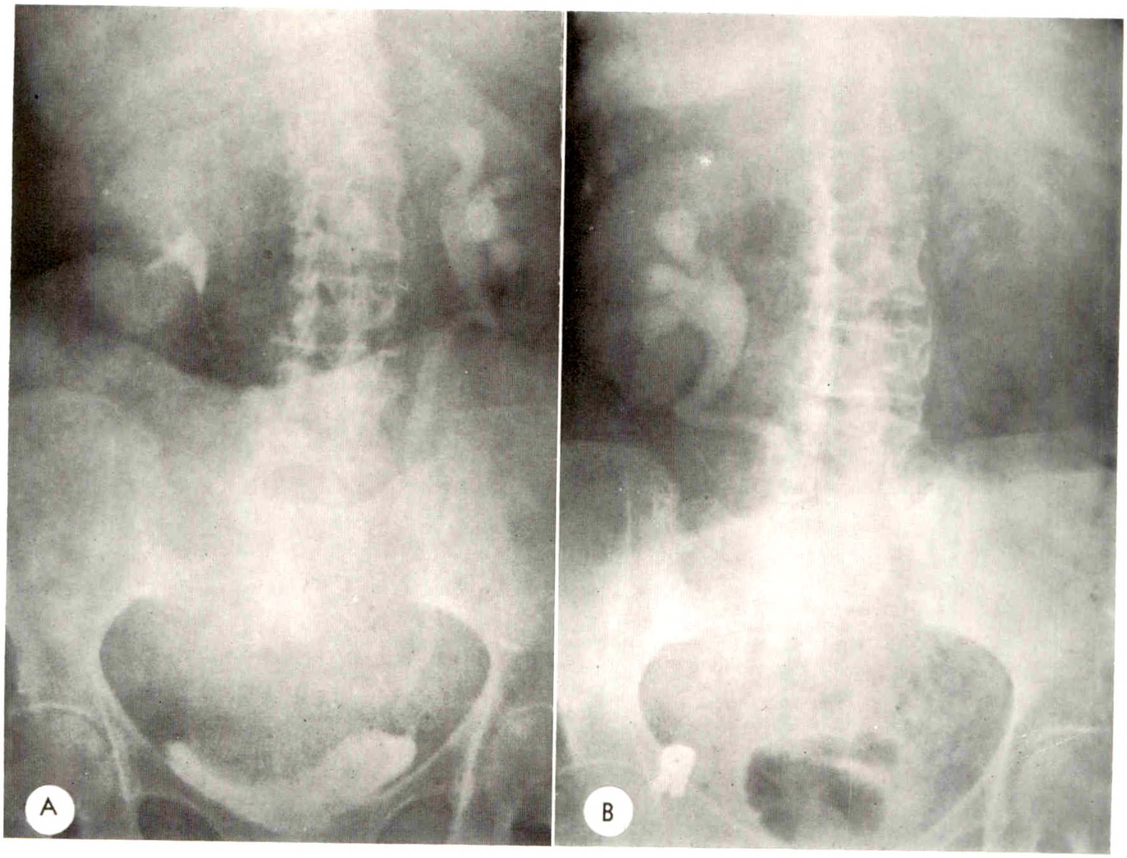
FIG. 4. Case IV. (*A*) Intravenous pyelogram showing partially obstructed left ureter and hydronephrosis. (*B*) Drip infusion pyelogram showing obstruction at the level of the right ureterovesical junction and nonvisualization of the left kidney, indicating complete left ureteral obstruction and autonephrectomy.

Fig. 3. Case iii. Drip infusion pyelogram showing a mass on both sides of the pelvis.



masses. It is interesting to note that the left-sided mass was in the same area as the lymph node deficit, confirming the lymphangiographic impression. Impression: Metastatic carcinoma on both sides of the pelvis, the mass producing ureteral obstruction on the right side and iliac lymph node replacement on the left side of the pelvis. This diagnosis was subsequently verified at pelvic laparotomy.

Case iv. G.B., a 78 year old Negro female, had undergone panhysterectomy and bilateral salpingo-oophorectomy in June, 1964, for a papillary cystadenocarcinoma of the left ovary. Multiple pelvic implants were noted. Intravenous pyelography at that time revealed a partially obstructed left ureter and hydronephrosis (Fig. 4*A*). The right kidney and ureter were normal. In early October of the same year this patient was readmitted in car-



diac decompensation and azotemia. The blood urea nitrogen was 104 mg. per 100 ml. and serum creatinine was 22.0 mg. per 100 ml. A DIP study, performed shortly after this admission, revealed an obstruction at the level of the right ureterovesical junction and nonvisualization of the left kidney, indicating complete left ureteral obstruction and autonephrectomy on this side (Fig. 4*B*). A right nephrostomy was performed. The patient has since been lost to follow-up.

Case v. E.L., a 65 year old white female with a known history of inactive pulmonary tuberculosis of long duration, was admitted to this hospital on an emergency basis because of left upper quadrant abdominal pain. A routine roentgenogram of the abdomen revealed rather bizarre calcifications overlying the left renal area. Intravenous pyelography was performed which revealed nonfunction of the left kidney and a normal but somewhat rotated right kidney (Fig. 5*A*). Neither ureter was clearly demonstrated but a small portion was thought to be visible near the right ureteropelvic junction. Because it was still not certain as to the location of the renal calcifications, a DIN examination was performed. This revealed a horseshoe kidney with hydronephrosis on the left side (Fig. 5*B*). The calcifications were found to be located within the left kidney. These were thought actually to represent a calcareous and probably tuberculous pyelonephritis. Contrast material was demonstrated within and surrounding these calcareous deposits. It developed that what was thought to be the right ureter on the intravenous pyelogram in truth was a medially diverted calyx of a horseshoe kidney. No proof was obtained of the tuberculous nature of the renal calcification as the patient is still alive and her urine has remained sterile.

Case vi. G.D., an 88 year old white male,

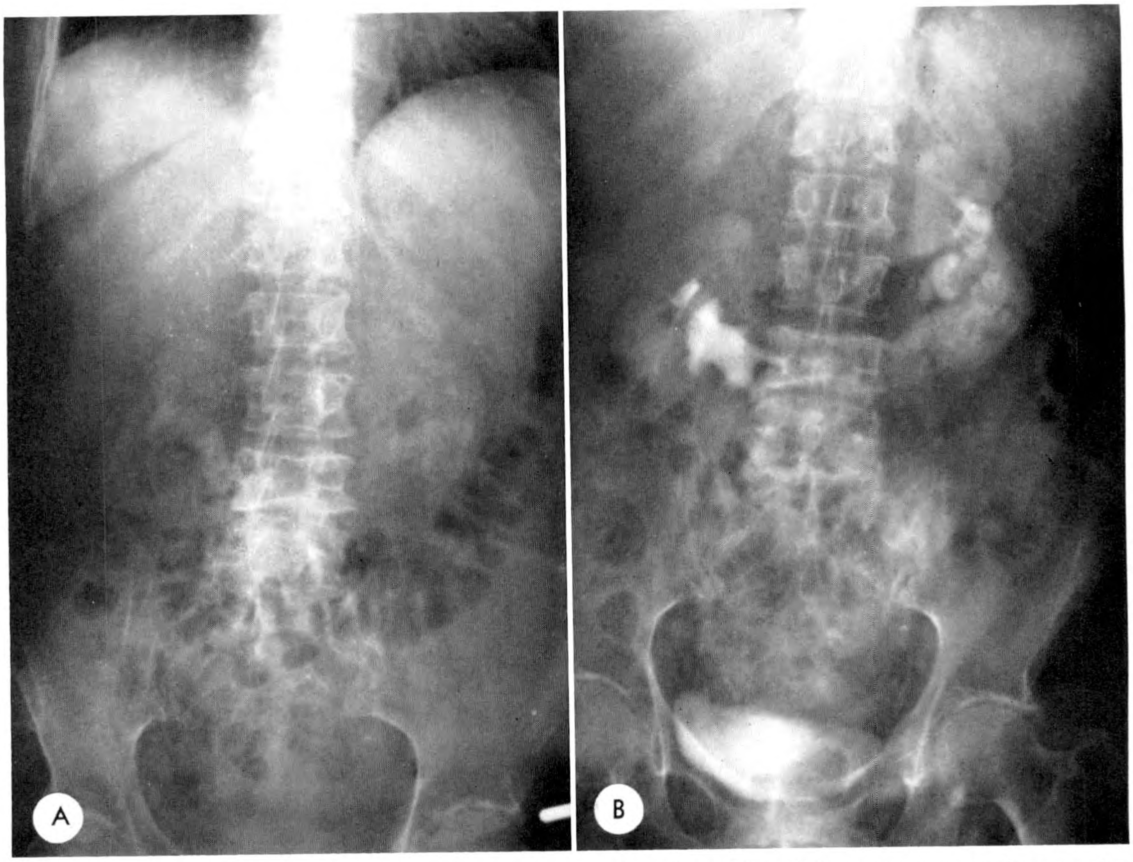


Fig. 5. Case v. (*A*) Intravenous pyelogram showing nonfunction of left kidney and a normal, somewhat rotated, right kidney. (*B*) Drip infusion pyelogram showing a horseshoe kidney with hydronephrosis on the left.

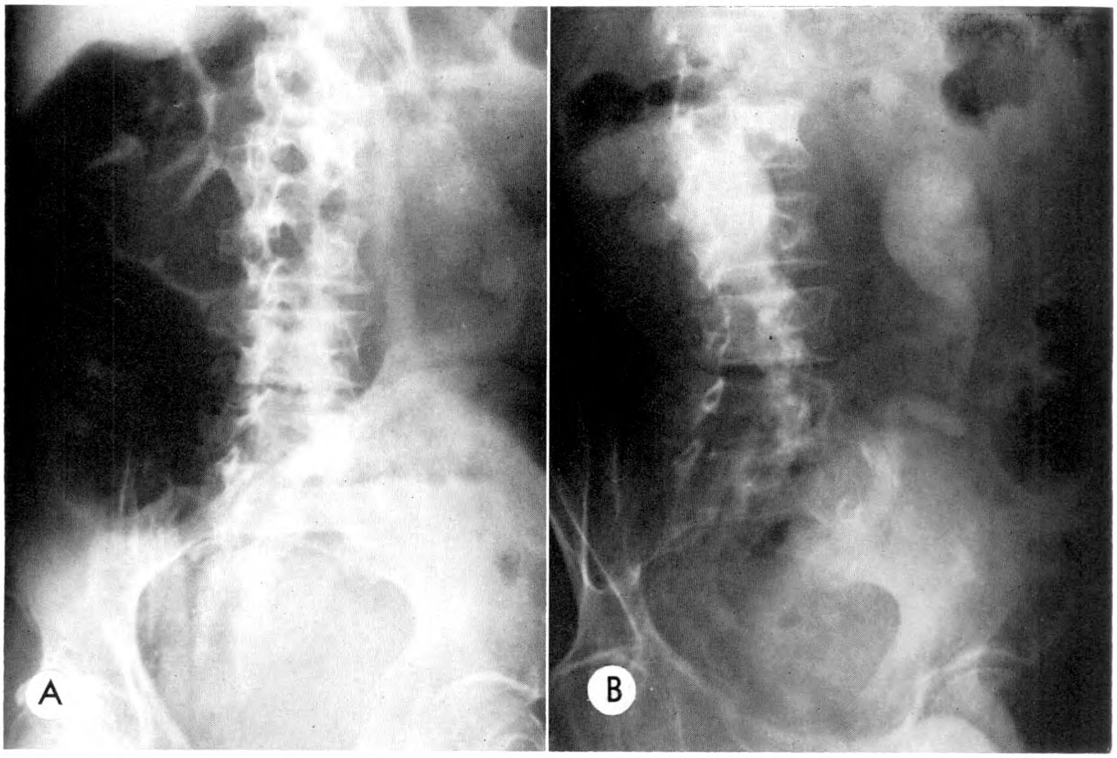


FIG. 6. Case VI. (*A*) Intravenous pyelogram showing left hydronephrosis but the actual point of obstruction is not demonstrated. (*B*) Drip infusion pyelogram showing massive bilateral hydronephrosis with dilated ureters proximal to the ureterovesical junction.

had undergone a resection of prostatic carcinoma in 1963. He re-entered this hospital in November, 1964, because of signs of both acute and chronic obstructive uropathy. Intravenous pyelography revealed a left hydronephrosis but the actual point of obstruction was not demonstrated (Fig. 6*A*). Nonfunction of the kidney was exhibited on the right. Blood urea nitrogen was 82 mg. per 100 ml. and serum creatinine was 6.2 mg. per 100 ml. The patient's daily urinary output was 900 to 1,500 ml. A DIP study revealed massive bilateral hydronephrosis with dilated ureters proximal to the ureterovesical junction. The bladder was massive, in keeping with a large volume of residual urine (1,500 cc.) and the palpably enlarged prostate indentation was demonstrated (Fig. 6*B*).

CASE VII. M.H., a 42 year old white female, re-entered this hospital for a possible pelvic exenteration. In the past, the patient had had radiation therapy for carcinoma of the cervix and now she had returned with clinically obvious advanced recurrent tumor. Intravenous pyelography revealed hydronephrosis of the right kidney due to incomplete obstruction at the ureterovesical junction. The left renal collecting system was not visualized. A DIP examination revealed the level of the right-sided obstruction but failed to demonstrate the left kidney (Fig. 7*A*). This finding indicated autonephrectomy on this side, resulting from prolonged and complete obstruction. Lymphangiography revealed abnormal lymph nodes in the right middle common iliac and right retroperitoneal (para-aortic) groups (Fig. 7*B*). The right internal common iliac lymph nodes were not visualized, suggesting complete replacement. Laparotomy subsequently confirmed the presence of tumor obstructing the ureterovesical junction and involving the bilateral iliac chains and retroperitoneal para-aortic lymph nodes on the right.

CASE VIII. P.J., a 20 year old white male, had had bilateral neoureterostomy in the past because of bilateral ureterovesical junction obstruction. Intravenous pyelography demonstrated massive hydronephrosis of the left kidney but there was no visualization of the right kidney even in 24 hour studies. Voiding cystourethrography demonstrated right-sided reflux

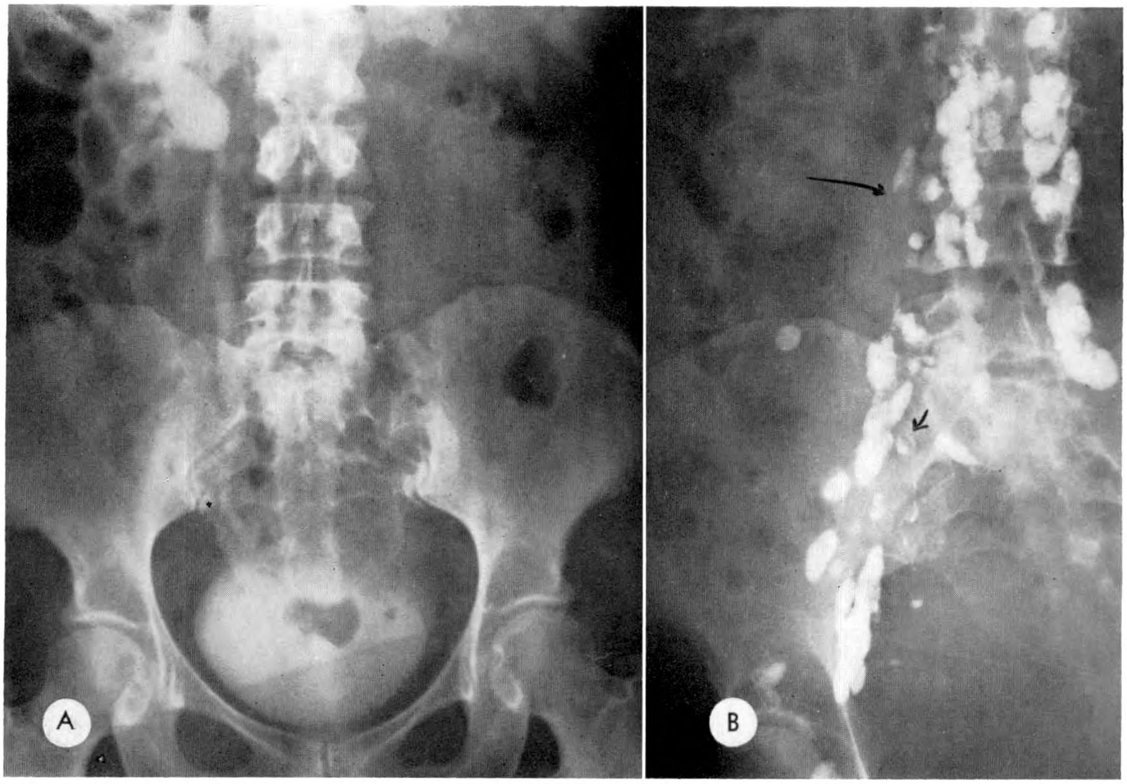


Fig. 7. Case vii. (*A*) Drip infusion pyelogram showing the level of the right-sided obstruction and no visualization of the left kidney. (*B*) Lymphangiogram showing abnormal lymph nodes in the right middle common iliac and right retroperitoneal groups.

only. A DIP study demonstrated massive bilateral hydronephrosis, with a differential in volume between the two sides, as might be expected (Fig. 8). It is of interest to note that the right side was partially visualized after 5 minutes, and the drip infusion pyelogram shown in Figure 8 was taken after 90 minutes. At that time the distal right ureter was identified.

Case ix. D.R., a 56 year old white male, entered this hospital in January, 1965, with complaints of joint pains. His blood urea nitrogen was 62 mg. per 100 ml. and serum creatinine was 4.0 mg. per 100 ml. Intravenous pyelography, performed shortly after admission, revealed poor concentration of the contrast material bilaterally. Casts and red blood cells subsequently were noted in the urine. A DIP examination, carried out 9 days later, revealed bilaterally enlarged kidneys (each 17 cm. in greatest diameter) with normal collecting systems (Fig. 9). Impression: Subacute glomerulonephritis with acute exacerbation.

Case x. G.D., a 73 year old white male, had undergone resection of recurrent colonic adeno-

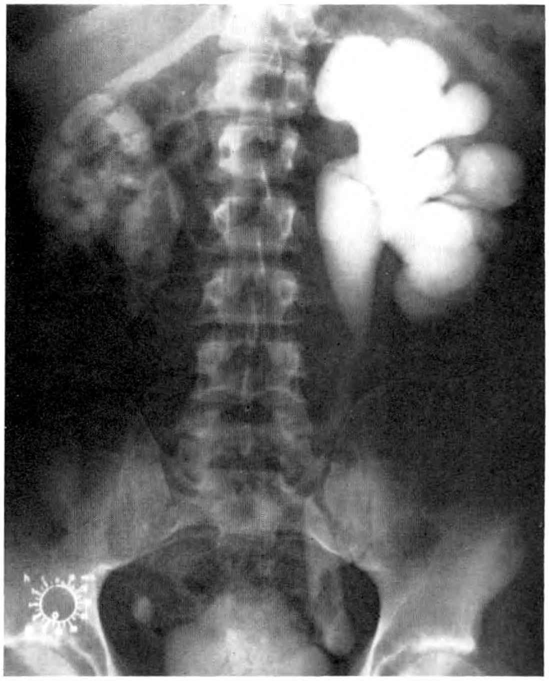


Fig. 8. Case viii. Drip infusion pyelogram showing massive bilateral hydronephrosis.

carcinoma in January, 1965. At the time of surgery, the left ureter was partially resected because of secondary tumorous involvement and a ureteroureterostomy was performed. Postoperatively the patient's urine remained clear. After discharge, however, an evaluation of the anastomosis was thought desirable. Instead of a retrograde study, a DIP examination was performed (Fig. 10). It revealed the left ureter as grossly normal in appearance with only moderate dilatation of the left intrarenal collecting system.

Case xi. N.O., a white female 23 years of age, had a long history of renal problems ("Bright's disease" twice during her teens, as well as enuresis with frequency of urination). In February, 1965, the patient was admitted because of functional uterine bleeding and anemia (hemoglobin 10.5 gm., and hematocrit 36 per cent). Her blood urea nitrogen was 159 mg. per 100 ml. and serum creatinine was 9.5 mg. per 100 ml. There was 3 plus albuminuria. Her blood pressure was 130/100 mm. Hg. A clinical diagnosis of chronic glomerulonephritis was entertained. A DIN study was performed to rule out the possibility of surgically correctable uropathy. This examination revealed diminished concentration of the contrast material, but normal parenchyma and collecting systems (Fig. 11). Impression: Changes compatible with chronic renal disease probably of a glomerulonephritic nature. (Unfortunately, this study reproduces poorly but it is included in order to demonstrate the usefulness of DIP examination in a patient presenting a markedly elevated level of blood urea nitrogen.)

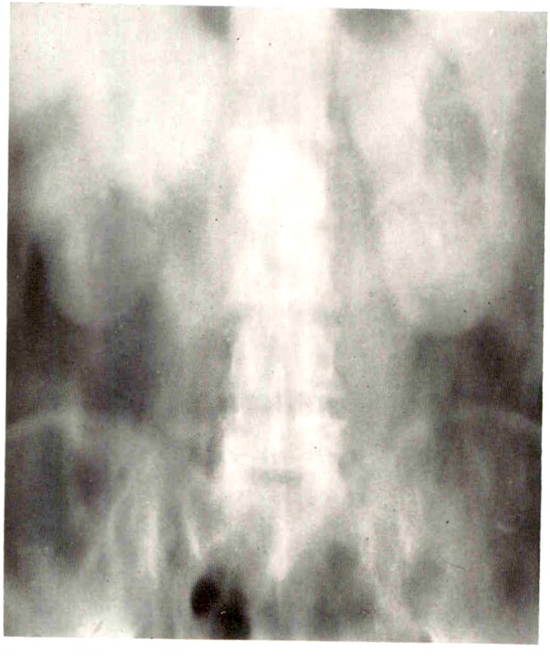


Fig. 9. Case ix. Drip infusion pyelogram showing bilaterally enlarged kidneys with normal collecting systems.

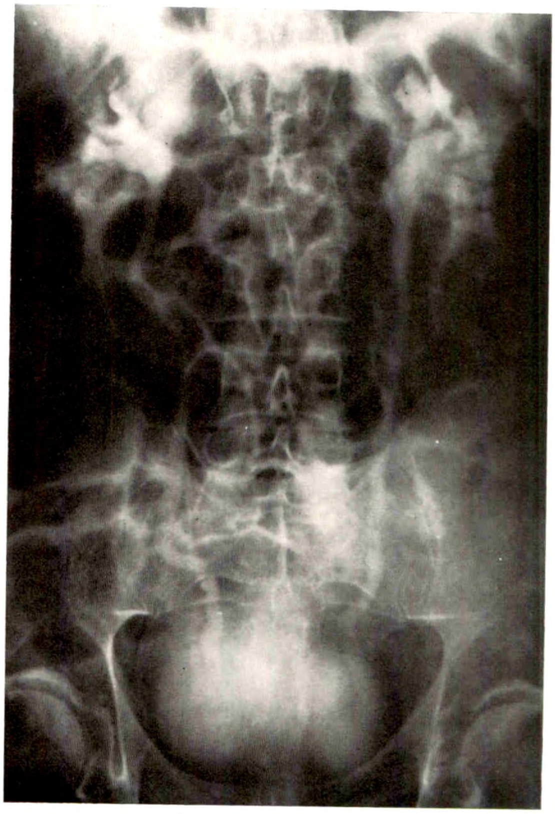


Fig. 10. Case x. Drip infusion pyelogram showing a grossly normal left ureter and only moderate dilatation of the left intrarenal collecting system.

Case xii. A.H., a white female 57 years old, entered the hospital with a chief complaint of increase of abdominal girth of 1 year's duration. She was known to have diabetes mellitus and hypertension, with moderate anemia (hemoglobin 10.2 gm., hematocrit 34 per cent). Intravenous pyelography at another hospital yielded no visualization of the right kidney and ureter and poor visualization of the left renal collecting system. Blood urea nitrogen at that time was 56 mg. per 100 ml. Upon transfer of the patient to this hospital, the blood urea nitrogen was still 56 mg. per 100 ml. and serum creatinine was 3.0 mg. per 100 ml. Intravenous pyelography this time failed to visualize either side. A DIP study was performed (Fig. 12). It re-

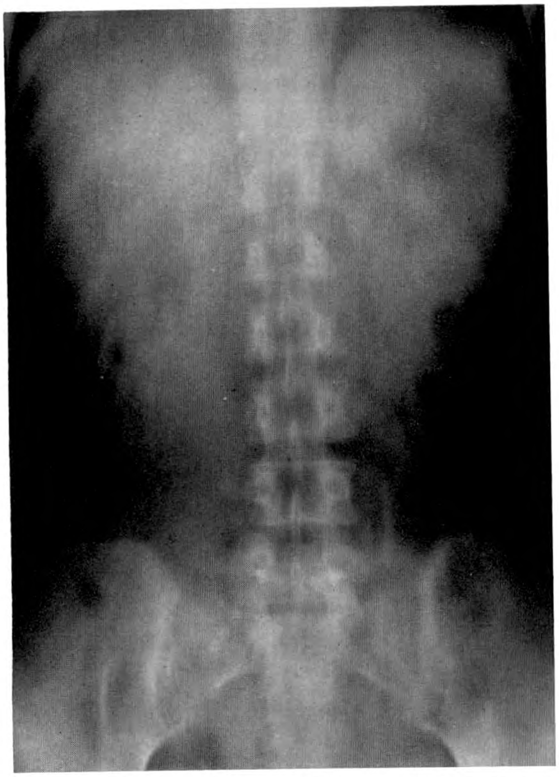


Fig. 11. Case xi. Drip infusion nephrotomogram showing diminished concentration of the contrast material but normal parenchyma and collecting systems.

vealed small kidneys: 6.5×5.5 cm. on the right and 9.2×4.5 cm. on the left side. The calyces were slightly blunted but not dilated. Both ureters were normal. Impression: Changes compatible with chronic glomerulonephritis, and possibly a superimposed pyelonephritis of subacute or chronic nature.

Case xiii. M.H., a 56 year old white female with chronic organic brain syndrome, was admitted to this hospital because of abdominal pain of vague nature. Serum calcium was 3.8 mEq./L.; serum phosphate, 3.1 mEq./L. Blood urea nitrogen was 47 mg. per 100 ml.; and serum creatinine was 2.2 mg. per 100 ml. There was poor visualization of both kidneys and no visualization of the renal collecting systems on either side by intravenous pyelography. A DIP study showed irregularly shaped kidneys and normal collecting system (Fig. 13). (The latter were clearly demonstrated at the end of 5 minutes.) Impression: Chronic glomerulonephritis; no surgical uropathy demonstrated.

RESULTS

The diagnosis reached in the 26 DIN studies to differentiate renal cysts from renal tumor subsequently were found to be correct at surgery and/or necropsy in 25 (96 per cent) of these examinations. The one instance in which an incorrect diagnosis was made was that of an Oriental male who was thought to have a large tumor of the right upper renal pole. In truth, he was proven first at surgery and later at autopsy to have had a large hepatoma which overlay and engulfed the renal cortex with so much contrast-laden hepatic mass that the roentgenographic technique used in the examination could not demonstrate what was left of the perirenal fatline in this extremely emaciated patient.

In the 84 studies undertaken to attain

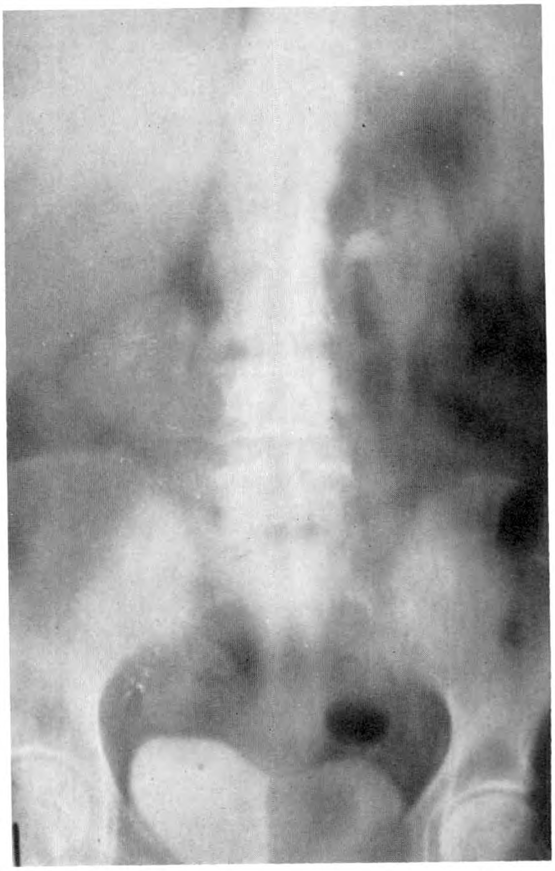


Fig. 12. Case xii. Drip infusion pyelogram showing small kidneys and slightly blunted but not dilated calyces.

better visualization of suspected renal areas than had been obtained with previous intravenous pyelography, better delineation and clarification of these areas were obtained in all cases.

An accurate appraisal was made in all cases of frank renal incompetence as to whether the condition was correctable by surgery. It should be emphasized that this group comprised 21 patients with blood urea nitrogen levels ranging from 26 to 159 mg. per 100 ml. and concentrations of serum creatinine varying from 1.9 to 22.0 mg. per 100 ml. Moreover, the DIP or DIN technique was performed in every case without untoward effect. A list of the diagnoses in these patients is given in Table I.

TOXICITY AND COMPLICATIONS

A test dose of 1 ml. of contrast agent was routinely given and a period of approximately 60 seconds was allowed to elapse before the main infusion was begun. To date, no fatalities or serious reactions have occurred.

Seven patients experienced a generalized "warmth" during DIP or DIN examinations. Seven other patients had nausea, and of these only 1 vomited. (These are side effects which commonly occur following the administration of the recommended routine intravenous diagnostic dose of methylglucamine diatrizoate 60 per cent. The incidence in the infusion technique does not appear to exceed that encountered at the routine dosage.) Three additional patients required the intravenous administration of diphenylhydramine 50 mg. during or at the end of the procedure because of itchy eyes (1), nausea, emesis, and generalized warmth (1) and shaking chills (1). The only treatment given to the other patients who experienced warmth, nausea, and vomiting, was reassurance.

In no case did the procedure have to be discontinued, and in only 1 case was the rate of infusion deliberately reduced and this from the very outset, because of the questionable cardiovascular status of the patient. In this patient the infusion was given over a period of 15 minutes, and no untoward effects were encountered.

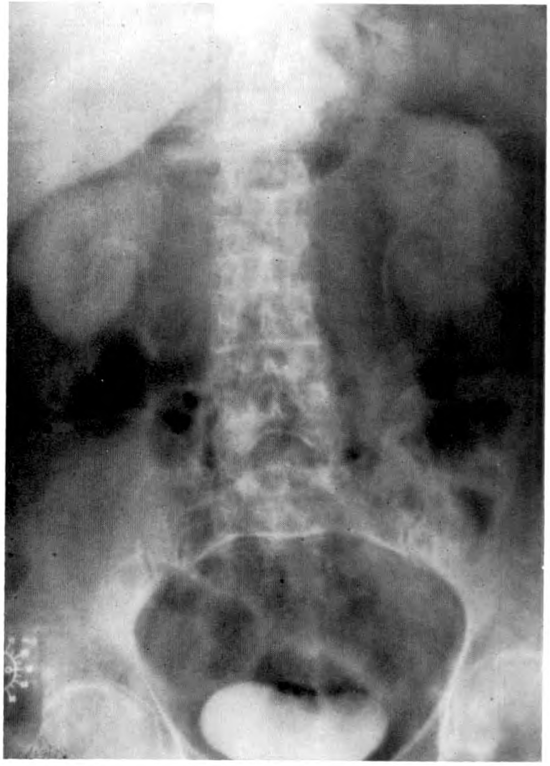


Fig. 13. Case xiii. Drip infusion pyelogram showing irregularly shaped kidneys and normal collecting system.

We have used 5 per cent glucose in water as the diluent in all cases except in patients with diabetes in whom normal saline has been used. Perhaps this precaution is unnecessary, however, since the total amount of glucose administered is fairly insignificant even in diabetic patients.

DISCUSSION

In our experience infusion-type pyelography combined with nephrotomography, whenever indicated, has proven to be safe, useful and reliable in the differentiation of renal cysts from renal tumors. In addition, we have found these studies to be of great diagnostic value, both as a safe and simple adjunctive procedure in a number of other conditions and situations as follows:

1. Evaluation of obscure renal outlines, such as the horseshoe, or dromedary type of kidney.

TABLE I

DIAGNOSIS IN PATIENTS WITH FRANK RENAL INCOMPETENCE WHO WERE STUDIED BY THE DIN OR DIP TECHNIQUE

Patient No.	Diagnosis	Age	Sex	Blood Urea Nitrogen (mg./100 ml.)	Creatinine (mg./100 ml.)
6	Pyonephrosis, Polycystic Kidney Disease, Anuria	65	M	100	12.6
40	Idiopathic Uremia	70	M	60	7.0
42	Cancer of Bladder with Ureterovesical Junction Obstruction	70	M	116	4.2
52	Acute Pyelonephritis	50	M	40	8.0
54	Ovarian Cancer with Pelvic Implants, Right Ureteral Obstruction, Left Autonephrectomy	78	F	104	22.0
59	Cancer of Prostate with Bilateral Ureterovesical Junction Obstruction	56	M	78	5.5
66	Nonsurgical Uropathy of Unknown Type	76	M	57	1.9
67	Cancer of Prostate with Bilateral Ureterovesical Junction Obstruction	88	M	82	6.2
69	Multiple Congenital Anomalies	8	M	92	4.3
72	Renal Tubular Necrosis	50	F	78	9.2
73	Cancer of Cervix, post-Wertheim Procedure, Bilateral Ureterovesical Junction Obstruction	35	F	42	2.5
77	Agenesis of Left Kidney, Chronic Pyelonephritis of Right Kidney	44	M	104	12.0
88	Chronic Pyelonephritis	36	F	51	9.5
93	Subacute Glomerulonephritis with Acute Exacerbation	56	M	62	4.0
94	Left Ureteropelvic Obstruction by Fibrous Band	84	F	57	2.4
97	Chronic Pyelonephritis	62	F	90	2.8
100	Chronic Glomerulonephritis	23	F	159	9.5
101	Cancer of Bladder with Bilateral Ureterovesical Junction Obstruction	69	M	26	5.0
105	Right Nephrectomy after Shotgun Wound with Renal Artery-Portal Vein Traumatic Shunt	29	M	138	17.8
106	Cancer of Prostate, Bilateral Ureterovesical Junction Obstruction	86	M	53	2.6
110	Acute Glomerulonephritis	36	F	57	6.2

2. Evaluation of the liver, spleen, and adrenal glands, since these organs are often clearly demarcated during the study due to the content of contrast material in their great vascular bed.

3. Diagnostic studies in infants and children, since the desired information can frequently be obtained at a faster rate, using fewer roentgenographic exposures than with routine intravenous pyelography; hence, the total radiation exposure to the patient is reduced.

4. Identification of the exact point of obstruction (stone, tumor). With DIP it is possible to identify the point of obstruction in a shorter length of time than with routine intravenous pyelography; it is also possible to identify this point in far less time and with less risk and effort than with retrograde studies.

5. Full visualization and evaluation of both ureters is possible with DIP without the need for retrograde examinations. This procedure, therefore, reduces the potential morbidity from anesthesia, infections and trauma associated with urinary tract instrumentation.[1,4,5,8]

6. Antegrade cystographic studies by the DIP technique are quite satisfactory since the concentration of contrast material within the bladder is high enough to provide diagnostic roentgenograms. Although not attempted yet, the possibility of voiding urethrograms using this technique deserves evaluation.

7. Accurate differentiation between surgical and medical uropathies.

8. Accurate appraisal of the renal status in patients in whom routine intravenous pyelography has failed to visualize one or both kidneys. This is especially true in patients with high levels of blood urea nitrogen and/or serum creatinine.

9. Treatment planning and follow-up evaluation in neoplastic disease. When DIP and DIN are combined with lymphangiography and/or inferior vena cavography, the maximum amount of information concerning the status and location of retroperitoneal structures is obtainable.

Although the present study is quite limited in total number of examinations carried out, the indications so far are that the DIP and DIN techniques appear to be quite safe and carry no greater risk of morbidity than routine intravenous pyelography.

Although no late complications have been experienced to date, a warning should be given concerning the use of the infusion technique in marginally or actually decompensated cardiac patients. The rate of infusion should be slowed in this type of patient so as to prevent possible overtaxing of an already embarrassed cardiovascular system.

SUMMARY

1. Our experience with drip infusion pyelography and/or nephrotomography in a series of 110 patients is described.

2. Methylglucamine diatrizoate 60 per cent, diluted with an equal amount of 5 per cent glucose in water, has proved to be the contrast agent of choice because it provides reliable diagnostic contrast and is both safe and economical in use.

3. The indications for use of the DIP and DIN technique are given.

4. The drip infusion technique used in these studies has proved to be a valuable diagnostic tool and is advocated for use in any private or institutional radiology practice.

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ADDENDUM

Since completion of this paper a patient, weighing 350 lb. with painless hematuria, was examined by the drip infusion technique using 350 ml. methylglucamine diatrizoate 60 per cent diluted with 350 ml. 5 per cent glucose in water. The time of infusion was 10 minutes, 2 seconds. The patient suffered no untoward effects and had no nausea or other reaction.

The author would like to express his sincere

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SIMPLIFIED NEPHROTOMOGRAPHY*

THE DRIP INFUSION TECHNIQUE

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NEPHROTOMOGRAPHY, as devised by Evans *et al.*[2] in 1954, has proven to be an accurate method for differentiating renal cysts from tumors. It has also been useful in differentiating intrarenal from extrarenal pathology and in better defining calyceal deformities of varying etiologies.

While its diagnostic value has been established, technical difficulties have limited the general acceptance and utilization of the procedure. Tomography of the kidneys must be performed during a period of short-lived renal parenchymal opacification (nephrographic phase). Satisfactory studies, which are often time consuming, require technical skill and experience and are dependent upon precise timing and careful attention to detail.[1,10,13] Simplification is desirable.

Intravenous infusion of a large volume of dilute contrast material produces a dense and long lasting nephrogram.[9] This technique greatly simplifies nephrotomography and extends its practical application. This method, referred to as drip infusion nephrotomography, is the subject of this paper.

HISTORICAL REVIEW

Although Steinberg and Robb[11] noted opacification of the renal parenchyma during intravenous angiocardiography in 1938, it was not until 1951 that Weens *et al.*[15] utilized a practical intravenous technique specifically for nephrography. They injected 50 cc. of 70 per cent diodrast rapidly through a Robb-Steinberg needle and syringe and noted that the nephrogram, which rapidly faded, was best filmed at 15 to 18 seconds after the injection. They suggested application of the method to the differention of renal cysts from tumors, but had no pathologic material of their own. Wall and Rose[14] modified this technique only slightly, and reported opacification of the kidneys in 100 per cent of 80 cases. They also noted opacification of the aorta and the renal arteries in 50 per cent of cases, but felt that this large vessel visualization was not good enough to be of great value and still preferred translumbar or retrograde femoral aortography for problems of renal masses.

In 1954, Evans *et al.* added body-section roentgenography to nephrography and called the method nephrotomography. Tomography, by eliminating bowel gas and opacified renal parenchyma at levels overlying and otherwise obscuring an intrarenal lesion, clearly demonstrated cysts as well defined radiolucent areas, while tumors appeared as densities. With further experience, this differentiation was found to be 94 to 95 per cent accurate[1,4] and the evaluation of renal masses became the prime indication for nephrotomography. Diagnostic criteria have been fully described.[1,3,4,16]

The Evans group found that by using a decholin circulation time as a guide they could visualize contrast material in the aorta and renal arteries in 75 per cent of cases. This intravenous aortogram, although not essential for diagnosis, was at times helpful and it is included in their currently recommended technique. The technique, in brief, is as follows:

1. Take test tomograms
2. Insert Robb-Steinberg needle (12 gauge)
3. Determine circulation time (decholin)
4. Inject 30 cc. of 50 per cent hypaque
5. *Rapidly* inject 50 cc. of 90 per cent hypaque (1–1.5 seconds)

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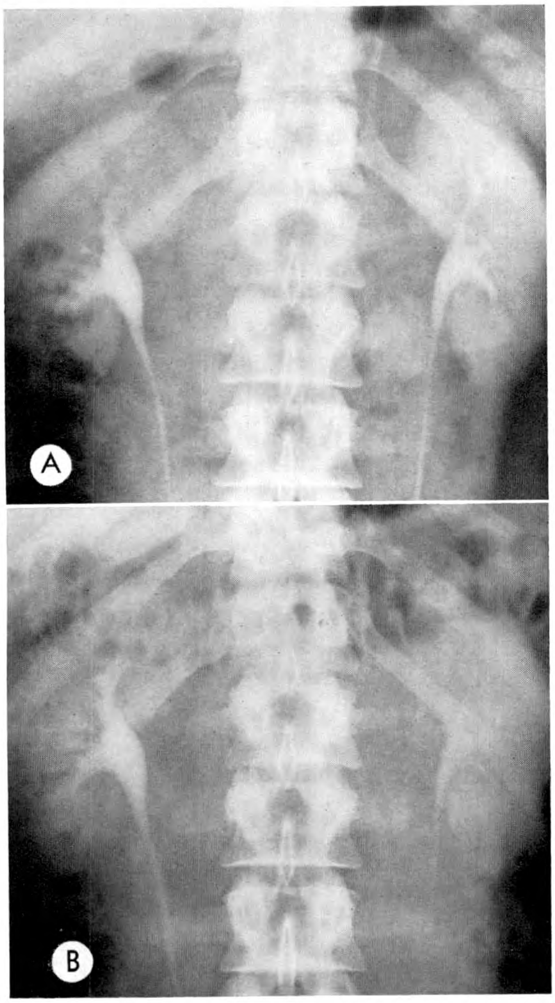

FIG. 1. Drip infusion nephrography. (*A*) Good bilateral nephrogram at 10 minutes from the start of the infusion. (*B*) Decreased but satisfactory nephrogram at 45 minutes.

6. Take conventional roentgenogram at predetermined circulation time, followed by several tomograms.
7. Inspect films and re-inject without hesitation if further studies are needed

As indicated, technical skill and experience are required for optimal results. Placement of a 12 gauge needle is frequently difficult and surgical exposure of a vein is often a necessity. Precise timing and rapid exposures are prerequisites for success. Repeat injection is often necessary and the procedure, in most cases, demands an hour or more of the radiologist's time.

In 1960, Lowman and De Luca[7] described a simple method for obtaining a satisfactory nephrotomogram. They injected 50 cc. of 50 per cent hypaque over a period of 2 minutes through a 20 or 21 gauge needle, showing that a nephrogram could be produced without the use of a large bore needle and without rapid injection. However, their case material was limited and corroborating studies were not reported.

Recently, during studies designed to improve the quality of excretory urography, Schencker[9] infused large volumes of dilute contrast material intravenously. Excellent pyelograms were obtained and striking, long lasting nephrograms were evident in all cases. This nephrogram was denser than that obtained with the 50 cc. injection by Lowman and De Luca and, importantly, was prolonged, lasting up to 45 minutes after infusion (Fig. 1, *A* and *B*). This technique of drip infusion was applied to nephrotomography with gratifying results. Tomograms could be obtained in a deliberate manner; repeat sections when necessary did not require reinfusion. Problems in needle placement were eliminated. The study could be completed in less than 30 minutes and it rarely required more than a few minutes of the radiologist's time.

TECHNIQUE

A large volume of dilute contrast material (2 cc./lb. of 25 per cent hypaque*) is infused intravenously through an 18 gauge needle. The flow is unrestricted and the average infusion takes 6–10 mintues. The otpimal nephrogram appears at the end of the infusion. Tomograms are made and inspected, and if further information is needed they are repeated. The technique in detail is as follows:

1. The patient is not dehydrated.
2. The infusion solution is prepared: 1 cc. per lb. of 50 per cent hypaque is mixed with 1 cc. per lb. of 5 per cent dextrose in water in a standard infusion bottle (screw

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* Hypaque (diatrizoate sodium) was generously supplied by Winthrop Laboratories, New York, New York.

top bottles make preparation easy†). The minimal adult dose is 300 cc. of the resultant 25 per cent solution, and 400 cc. is generally sufficient for even the largest of subjects.

3. A scout tomogram is obtained at 7 or 8 cm. from the table top (supine position). The technical factors are adjusted as indicated. Low kilovoltage (60–70 range) and short time (2–4 seconds) favor contrast and improve quality.

4. The contrast solution is infused, without restriction, through an 18 gauge needle. The time necessary for completion of the infusion averages 6–10 minutes and is not critical. A smaller intravenous needle may be used (19 or 20 gauge).

5. Tomography is begun at the end of the infusion. While sections at 6, 7, and 8 cm. will suffice in most cases, we routinely obtain 6 tomograms at 5–10 cm. levels. Filming is not hurried. As previously described, adequate tomograms are obtainable for 45 minutes.

Less than the recommended amounts of 50 per cent hypaque and 5 per cent dextrose and water are at times satisfactory but do not allow for consistently optimal studies. The nephrogram apparently depends, not only upon a large amount of contrast material, but also upon adequate hydration and diuresis. The large urine flow (4–10 cc. per minute) induced during the infusion floods the system, causing filling and distention of the renal tubules. Contrast containing urine enters the tubules at a rate which exceeds their ability to empty into the renal pelvis, and a state of relative obstruction and tubular stasis is created. This stasis of contrast material in the renal tubules seems to account for the dense and sustained characteristics of the drip infusion nephrogram.

If the patient is dehydrated (because of his illness, etc.) prior to examination, a larger than usual volume should be administered. Very large volumes, however, do not seem to improve the studies, and for the present, the dosages as recommended seem to be optimal. A regimen for infants and children has not been worked out, but the general principles of an increased amount of contrast material and adequate hydration should be used as guide lines.

CASE MATERIAL

The case material was obtained from the U. S. Army Hospital, Fort Jackson, South Carolina and Brooke General Hospital, Fort Sam Houston, Texas. Sixty-one examinations have been performed to date. In all instances a satisfactory nephrogram was obtained. In 3 cases the studies were inadequate because of technical factors unrelated to the quality of the nephrogram. The diagnoses included: 20 benign cysts, 13 of which were verified at surgery; 3 carcinomas (proven at surgery); 12 calyceal deformities due to chronic pyelonephritis; 1 extrarenal tumor (retroperitoneal liposarcoma); 1 hydronephrosis; 2 calyceal deformities due to hypertrophied peripelvic fat; and 18 normal kidneys. In 1 case an opacified bulge on the lateral aspect of a left kidney was interpreted as a normal variation.[5] The patient, however, had hematuria and surgery was performed, at which time the "bulge" was found to be a carcinoma. This accounted for the only known misdiagnosis.

REACTIONS

No serious reactions have been encountered in this series or in a total of over 300 cases in which drip infusion has been used for pyelography. There have been only a few minor urticarial reactions. Nausea occurred with a frequency comparable to standard low dose intravenous pyelographic techniques.

APPLICATIONS

As with standard nephrotomography, the prime indication for this simplified technique is the differentiation of renal cysts from tumors. The value of this information in the selection of patients for surgery has been emphasized[1,2,3,7,10,16] but, as yet, remains controversial. Urologists are reluctant to rely completely upon a nephrotomographic diagnosis[6,8] and have generally preferred to corroborate the roentgen findings surgically.

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GUIDANCE IN PLANNING AND PERFORMING RENAL SURGERY

While its role in the selection of patients for surgery is incompletely defined, nephrotomography is of great value as a guide in planning and performing renal surgery. With a preoperative tomographic diagnosis of "cyst," the kidney can be thoroughly examined with less concern for the violation of fascial barriers and for the dissemination of malignant cells. The nephrotomogram, by indicating the exact size and location of the lesion, greatly facilitates exploration. Even if the cyst does not present on the kidney surface, it is easily found and studied through a well placed nephrotomy incision (Fig. 2, *A* and *B*). If there are no signs of malignancy, the kidney need not be resected.

With a preoperative nephrotomographic diagnosis of tumor, a radical procedure is planned and, after only minimal manipulation and external inspection, is carried out (Fig. 3, *A*, *B* and *C*). Nephrotomy is not performed. The patient is thereby offered the best possible chance for survival.

In addition to its use in the evaluation of renal masses, the simplicity of drip infusion nephrotomography makes it readily applicable to the routine preoperative study of patients scheduled for renal surgery of varying types.

Just as the general surgeon relies upon the upper gastrointestinal series, the barium enema study and the cholecystographic examination for valuable prelaparotomy information, so can the urologist benefit from nephrotomography. Unsuspected cysts, tumors and anomalies may be made

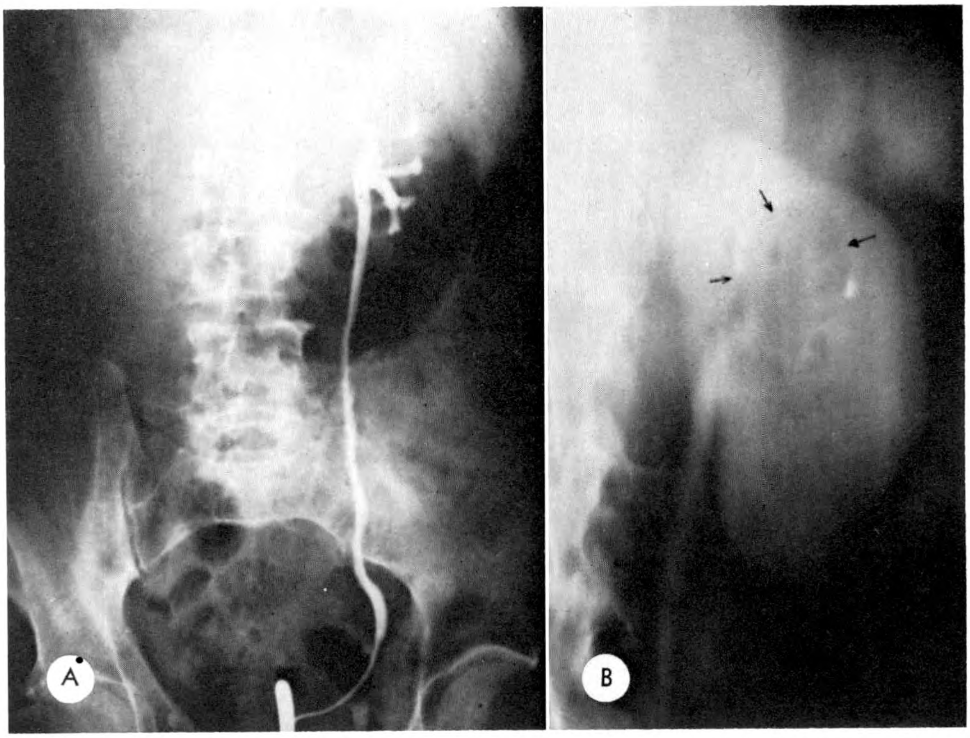

FIG. 2. A 66 year old male with hematuria. (*A*) Left retrograde pyelogram demonstrates a rounded deformity of the upper minor calyx. (*B*) Drip infusion nephrotomogram demonstrates a well defined lucency which is characteristic of a simple cyst. At surgery, the cyst was not visible or palpable; however, a nephrotomy incision in the proper area revealed a benign cyst. (Reproduced by permission of *Medical Times*.)

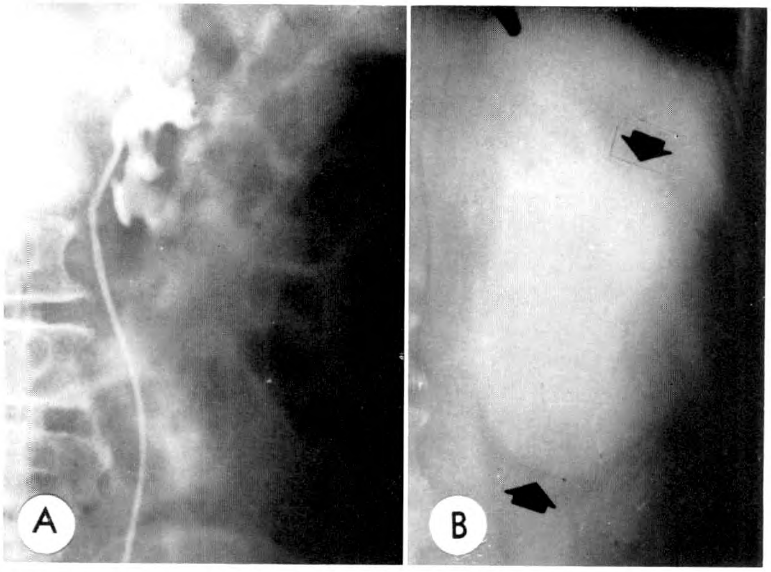

FIG. 3. A 57 year old male with left flank pain and hematuria. (*A*) Left retrograde pyelogram demonstrates a large mass in the lower pole of the kidney with displacement and deformity of the pelvis and calyces. (*B*) Drip infusion nephrotomogram outlines the mass as an area of dense opacification. There is no associated radiolucency. The tomographic diagnosis is tumor.

evident, enabling the urologist to perform the best possible procedure in each given case. The following case illustrates its value.

CASE I. D.B., a 51 year old male, had been followed by the Urology Service for gross total hematuria and left flank pain for 10 months. Initial and follow-up urograms demonstrated a 4×7 mm. calculus encysted in the lower minor calyx on the left (Fig. 4*A*). The associated infundibulum did not fill, but a definite pressure defect was not evident. At cystoscopy bloody efflux was noted at the left ureteral meatus.

Because of the persistence of symptoms and the fear of an underlying neoplasm, exploration and surgical resection were contemplated. A preoperative nephrotomogram was obtained. This clearly demonstrated two 4 cm. in diameter cysts in the lower pole of the left kidney (Fig. 4, *B* and *C*). These cysts appeared to compress the lowermost infundibulum between them, accounting for the infundibular narrowing and encystment of the calculus. Also noted was a small cyst in the right kidney.

Left partial nephrectomy with cystectomy was planned and carried out without complication. The patient has remained symptom free since surgery.

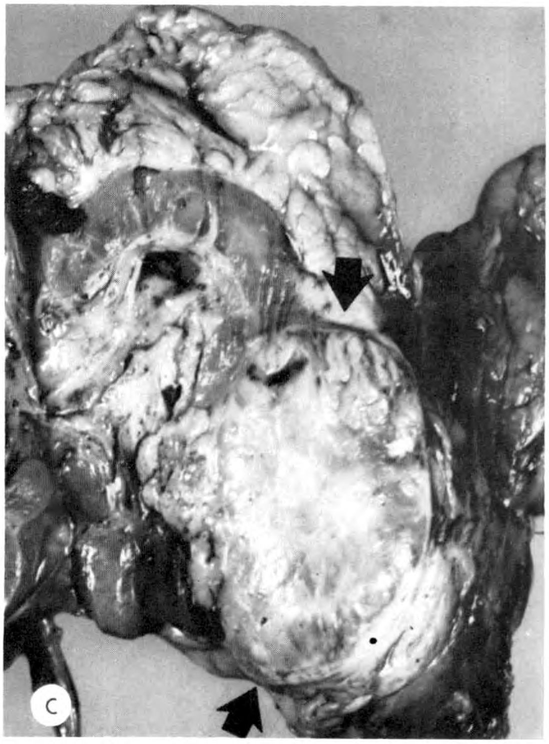

FIG. 3. (*C*) The pathologic specimen conforms closely to the roentgen appearance. The pathologic diagnosis was adenocarcinoma.

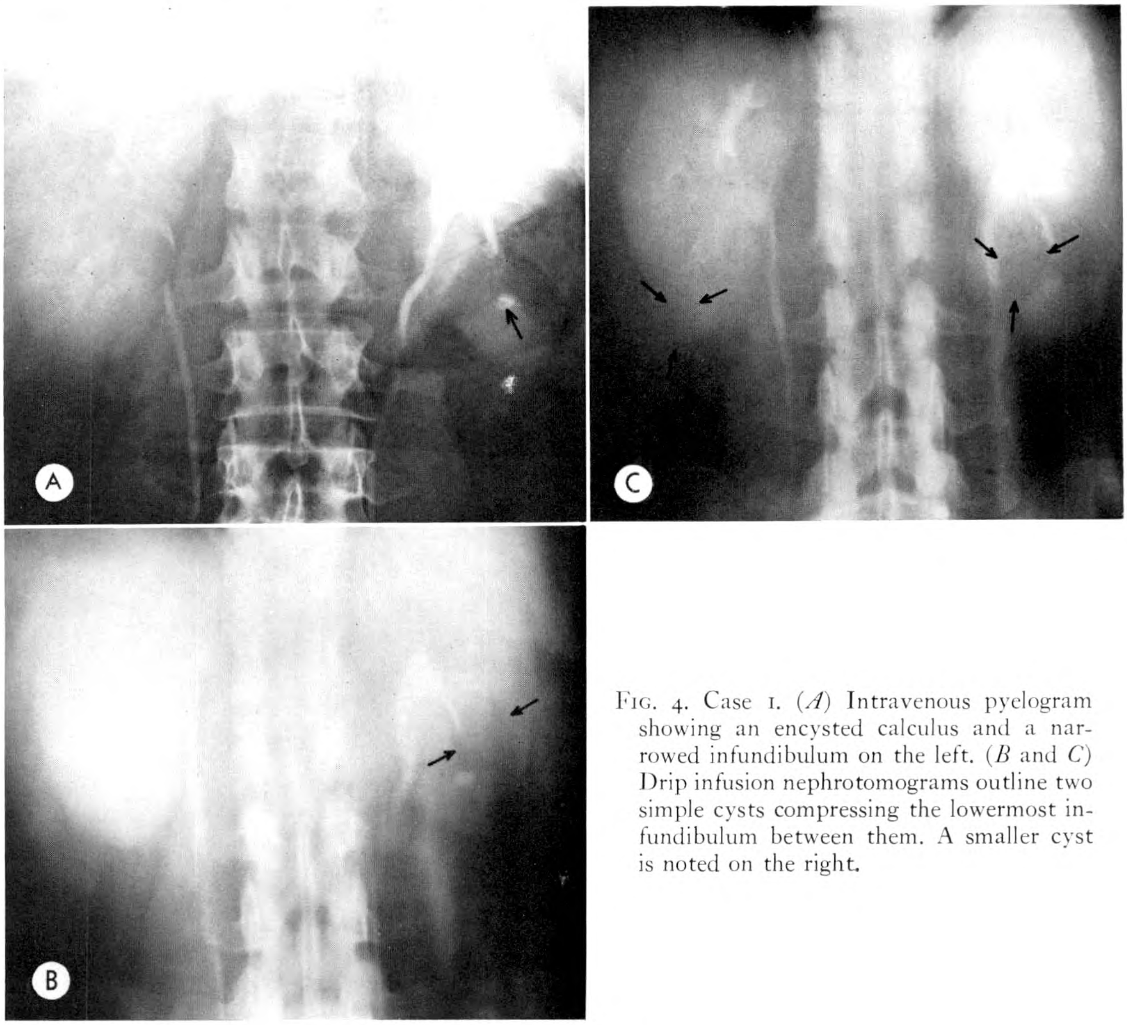

FIG. 4. Case I. (*A*) Intravenous pyelogram showing an encysted calculus and a narrowed infundibulum on the left. (*B* and *C*) Drip infusion nephrotomograms outline two simple cysts compressing the lowermost infundibulum between them. A smaller cyst is noted on the right.

ROUTINE EVALUATION OF PROBLEM CASES

In many instances, even after thorough clinical and urographic evaluation, renal disease may be incompletely or incorrectly defined. Problems of calyceal deformity and dilatation as well as irregularities in renal contour may be solved by nephrotomography. Again the simplicity of drip infusion makes this application practical. The following case of "pyelonephritis" serves to illustrate this application.

CASE II. L.O., a 34 year old female, gave a long history of repeated episodes of urinary tract infection manifested by fever, dysuria, backache and malaise. Excretory urograms had demonstrated bilateral pyelocalyceal deformity and dilatation consistent with chronic pyelonephritis.

During a recent episode another excretory urogram was made (Fig. 5*A*). While it showed no change over previous studies, there was greater dilatation on the left than on the right. A nephrotomogram was obtained (Fig. 5*B*). A large parapelvic cyst was clearly demonstrated on the left. It appeared to compress and partially obstruct the renal pelvis. Impaired drainage was evident on the retrograde study. Excision of the cyst was performed. While the patient continues to suffer from bouts of infection, it is hoped that the relief of obstruction will improve the over-all prognosis.

LIMITATIONS

Because the contrast material is not delivered in a bolus, an aortogram cannot be obtained with drip infusion. In some instances this may be a drawback. However,

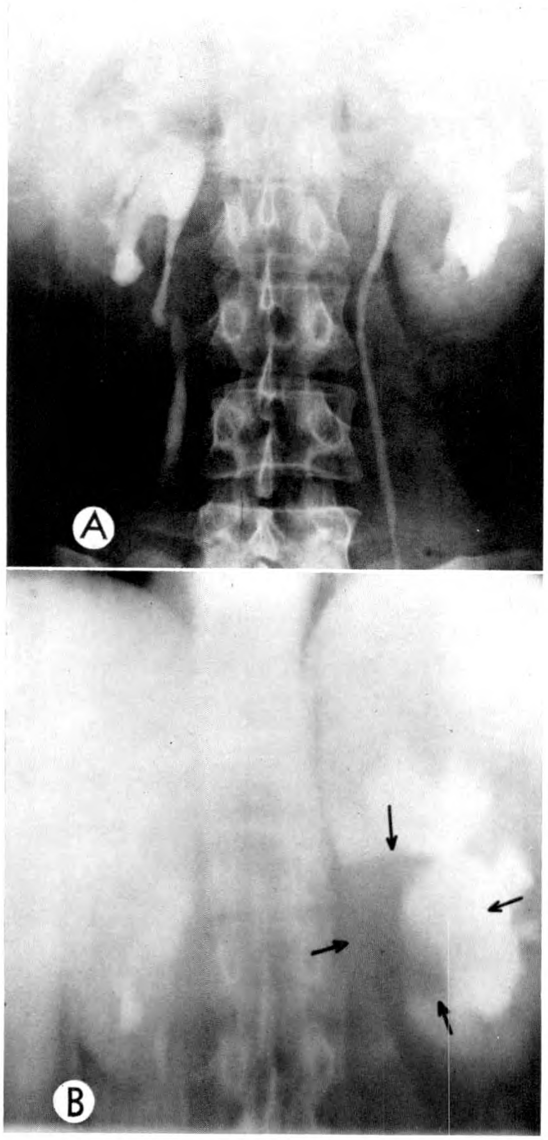

FIG. 5. Case II. (*A*) Intravenous pyelogram showing greater pyelocalyceal dilatation on the left than on the right. (*B*) Drip infusion nephrotomogram demonstrates a large parapelvic cyst compressing the renal pelvis on the left.

the intravenous aortogram often suffers from poor quality and is at times confusing. When combined with nephrotomography, it is rarely diagnostic in itself.[13] Its unavailability is, therefore, not considered to be a serious limitation. If, on occasion, nephrotomography leaves questions unanswered, it is best followed by selective renal arteriography as recommended by Tillotson and Halpern.[12]

CONCLUSIONS AND SUMMARY

Intravenous drip infusion of dilute contrast material, by producing satisfactory and sustained nephrograms without the technical difficulties inherent in rapid injection techniques, has greatly simplified nephrotomography. The drip infusion technique should encourage more general acceptance and utilization of nephrotomography. The technique, its theoretic aspects and limitations, and the broadened applications of nephrotomography are discussed.

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SELECTIVE RENAL ARTERIOGRAPHY IN MEDICAL DISEASES OF THE KIDNEY*

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ROENTGENOGRAPHIC demonstration of the renal arteries in the living was first achieved by the introduction of translumbar aortography in 1929 by dos Santos, Lamas and Pereira Caldas.[6] Renal arteriography was greatly advanced in 1953 by Seldinger[28] with the development of the percutaneous method of transfemoral arterial catheterization. Subsequent refinements in the technique permitting selective catheterization of the renal arteries (Ödman,[25] Edholm and Seldinger[7]) and the development of less toxic contrast media have made it possible to obtain arteriograms of sufficient detail to depict the small vessel changes in various diseases of the kidney.

In the past, selective renal arteriography has been used principally in the diagnosis of surgical diseases[10] of the kidney rather than those of a medical nature. The value of selective renal arteriography in the diagnosis of renal tumors,[3,8] cysts,[3,8] trauma[4] and lesions of the main renal arteries[22] has been stressed. However, little information is available regarding the arteriographic features of hypertensive vascular disease[22] and pyelonephritis,[30,31] particularly with regard to changes in the small renal arteries. This is surprising, as blood vessel changes that characterize primary vascular and certain parenchymal diseases of the kidney have been repeatedly demonstrated by postmortem renal arterial injection studies.[1,5,12,15,16]

In this study our primary interests have been directed to the evaluation of the small intrarenal arteries in the so-called medical diseases of the kidney. It has become apparent that there are distinguishable lesions of the small renal arteries present on the selective arteriogram which are not generally recognized by abdominal aortography, and that these lesions fit certain patterns which may be helpful in differentiating primary vascular from parenchymal disease of the kidney.

TECHNIQUES AND METHOD

During the past 3 years selective renal angiography has been performed on over 200 patients with a wide spectrum of renal diseases. The Seldinger method of percuteous transfemoral arterial catheterization has been utilized to introduce an Ödman Kifa catheter into the aorta, catheterizing the arteries to both kidneys whenever possible. A detailed description of the technique as used in our department has been reported by Foster.[9] Serial roentgenograms exposed at the rate of 2 per second for 4 seconds followed by 1 per second for 5 seconds were obtained using the Elema-Schönander rapid film changer, permitting demonstration of the arterial, capillary and venous phases of the circulation. In some patients roentgenograms were obtained for an additional 5 seconds. For most studies a hand injection of 6 to 8 cc. of 50 per cent hypaque or 60 per cent renografin was used, although in some patients with markedly contracted kidneys with a slow run-off as determined by test injections as little as 3 cc. was considered sufficient. On the other hand, in patients with a large highly vascular tumor when visualization of the renal veins is important, as much as 15 cc. may be required. We wish to stress that clinical judgment must be exercised in determining the amount of opaque material. Stereo-arteriography with successive injections has been helpful in a small number of patients, but it is not necessary in most instances. Roentgenograms in the oblique and upright positions[18] have been obtained in selected patients. In those cases in which there were multiple renal arteries, catheter aortography was performed. The presence of an accessory renal artery may be suspected by a ragged, sharply circumscribed filling defect on the nephrogram. In many instances, it was possible to selectively catheterize multiple arteries.

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I. THE NORMAL RENAL ARTERIOGRAM

A. ANATOMY

A detailed description of the normal arterial pattern has been given by Edsman,[8] Boijsen,[2] and Graves.[13] Briefly, the main renal artery divides at a variable point between the aorta and the hilus of the kidney into an anterior and posterior division, each division in turn giving rise to segmental arteries, usually 5 to 7 in number without collateral arterial blood supply between the segments. Many of the so-called aberrant or accessory arteries are segmental vessels with a precocious aortic origin. These segmental arteries divide in the kidney sinus into smaller branches which enter the parenchyma between the lobes of the kidney and are accordingly termed the interlobar arteries. These arteries pass along the walls of the calyces, following the pyramids to their bases and end by arching over them as the subcortical arcuate vessels. Numerous fine vessels—the interlobular arteries—are given off in the cortex. They course parallel to each other at right angles to the outer surface of the kidney, and are the parent vessels of the afferent arterioles[14] (Fig. 1 *A*).

B. ROENTGENOGRAPHIC FEATURES

In the normal selective arteriogram (Fig. 1 *B*), there are several characteristics worth emphasizing. There is an even distribution of large vessels which reduce in diameter with each bifurcation and extend well into

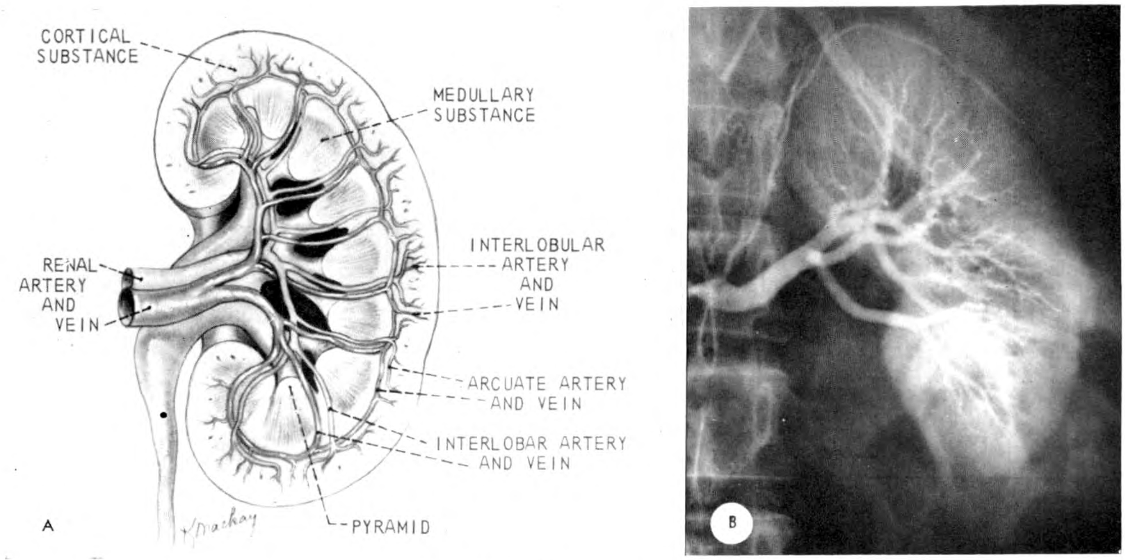


Fig. 1. (*A*) Diagram of renal circulation. (*B*) The normal renal arteriogram shows uniform vessels with smooth outlines and narrow angles at bifurcations.

the periphery of the kidney. The interlobar vessels are smooth in outline with gentle curves without tortuosity or narrowing. Narrow angles are formed at bifurcations. As the contrast medium is well concentrated in the renal vessels and opacification of other aortic branches is avoided, selective arteriography clearly shows vessels down to the arcuate size. Frequently, the interlobular arteries are visible in the cortex, presenting a characteristic radial pattern perpendicular to the renal surface. Not uncommonly, the segmental and interlobar arteries produce an imprint defect on the pelvocalyceal system as they cross. This phenomenon has been observed by Lim[19] as early as 1921.

Following the arteriographic phase, the nephrogram appears and is characterized by a diffuse opacification of the entire kidney which represents distribution of the contrast medium in the smallest vessels, the interstitial fluids and the tubular system.

The renal veins are opacified approximately 6 to 12 seconds after injection in the normal kidney and are superimposed upon the nephrogram.

II. PATHOLOGIC CONDITIONS

A. VASCULAR NEPHROSCLEROSIS

Three major conditions involving the blood vessels of the kidney are included under the term vascular nephrosclerosis:[29] (1) arterial nephrosclerosis, (2) arteriolar (benign) nephrosclerosis, and (3) the accelerated or malignant phase of hypertensive vascular disease.

1. *Arterial nephrosclerosis* (*arteriosclerosis*), for the most part, occurs in association with similar lesions in other vessels throughout the body. This condition has been studied both by selective renal arteriography and postmortem arteriographic injections of kidney specimens. The arteriogram reveals irregular filling defects (atheromatous plaques) at the origin of the renal artery that reduce the arterial lumen. The distal arterial branches are irregularly reduced in caliber by other plaques. The smaller arteries (less than 2 mm. in diameter) are usually not involved (Fig. 2).

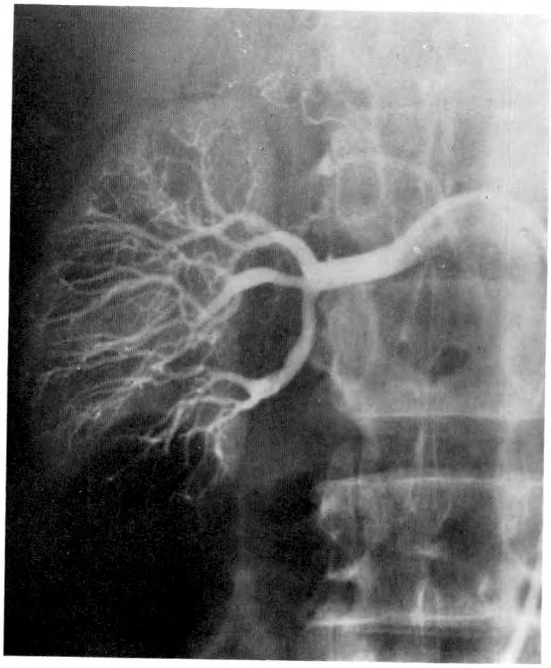


FIG. 2. Arterial nephrosclerosis and hypertension. Atheromatous disease is present in the primary and secondary branches of the renal artery. The small intrarenal arteries are uniformly narrowed.

2. *Arteriolar nephrosclerosis, also called benign nephrosclerosis*, is intimately associated with essential hypertension.[29] Histologically, the characteristic feature consists of a muscular hypertrophy of arterioles with hyalinization of the walls and narrowing of the lumens.

Postmortem arterial injection studies of kidneys have shown that there are roentgenographically detectable alterations in the arterial system of kidneys from hypertensive patients.[21] The selective arteriogram frequently depicts the vascular changes associated with hypertension. When hypertensive vascular disease is of mild degree, the selective arteriogram may be normal. In the more advanced cases, the interlobar arteries show a reduced caliber which may begin abruptly and terminate with wide angle bifurcations. Gradual curvatures are replaced with sharp angulations. Usually, there is a beaded appearance to the outlines of these arteries (Fig. 3 *A*). The kidney is generally only slightly reduced in size, and the total arteriogram suggests a reduced arterial volume with a normal renal mass (Fig. 3 *B*). A good cortical nephrogram is obtained, and the main renal arteries appear normal unless involved by arteriosclerosis. In a few instances, a localized delay of blood flow was evident.

3. *Malignant nephrosclerosis or accelerated hypertensive disease* is characterized by rapid renal failure, papilledema and uremia. Histologically, there is a hyperplastic intimal proliferation of the small arteries and arterioles that reduces the luminal size associated with a necrotizing arteriolitis with fibrinoid necrosis of the arteriolar wall. The lumen of many vessels is almost obliterated (Fig. 4).

The vascular changes are well shown in Figure 5, *A*, *B* and *C*. A postmortem normal renal arteriogram is compared with those of a patient dying from malignant nephrosclerosis. The kidney is contracted, and the small intrarenal arteries end abruptly with increased tortuosity. The cortical vessels are markedly reduced in number.

The selective renal arteriogram in this condition is highly characteristic and correlates well with postmortem arterial injections. The main renal arteries may be huge, and the interlobar and arcuate arteries have a gnarled appearance and are shortened abruptly with distal pruning. Serial studies reveal slow blood flow with persistent irregular small vessel filling. The cortical nephrogram is faint or absent and venous filling is poor (Fig. 6, *A*, *B* and *C*; and 7, *A*, *B* and *C*).

Selective renal arteriography has been performed in 2 patients with malignant hypertension superimposed upon a back-

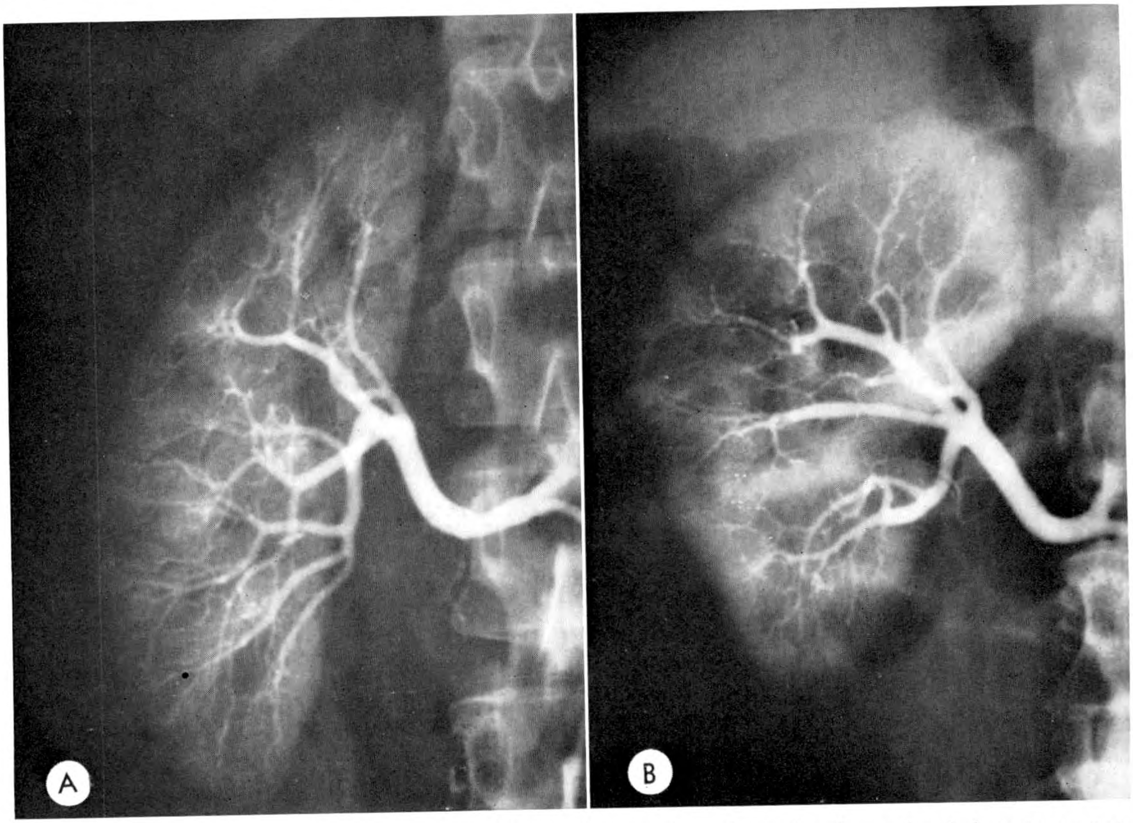
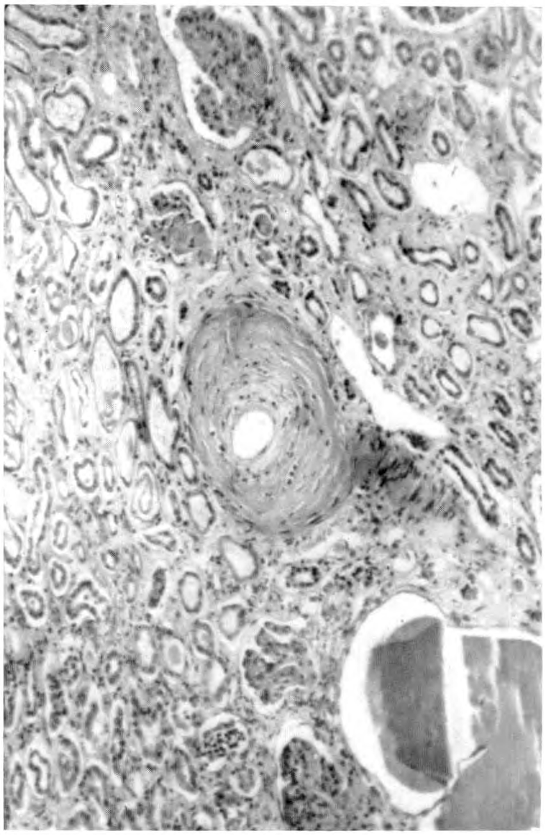


Fig. 3. Benign arteriolar nephrosclerosis. (*A*) The small parenchymal arteries show a beaded, tortuous pattern. (*B*) The interlobar arteries are markedly reduced in diameter with wide angle bifurcations.

FIG. 4. Malignant nephrosclerosis showing typical lamination and luminal narrowing of vessels with early fibrinoid changes.



ground of chronic glomerulonephritis. In each instance the arteriogram revealed a severe reduction in the finer vascularity of the kidney and marked decrease in cortical tissue, resulting in a leafless tree appearance (Fig. 8, *A* and *B*).

B. LESIONS OF THE MAIN RENAL ARTERY AND SEGMENTAL BRANCHES

1. *Main Artery Lesions.* Occlusive disease of the renal arteries has been classified by McCormack[20] into 6 distinct pathologic groups as follows: (a) the atherosclerotic plaque, (b) stenosis due to mural fibrosis of the vessel wall, (c) idiopathic thrombosis of the renal artery, (d) muscular hyperplasia, (e) idiopathic stenosis, and (f) dissecting aneurysm. The importance of these lesions has been well emphasized,[26] and

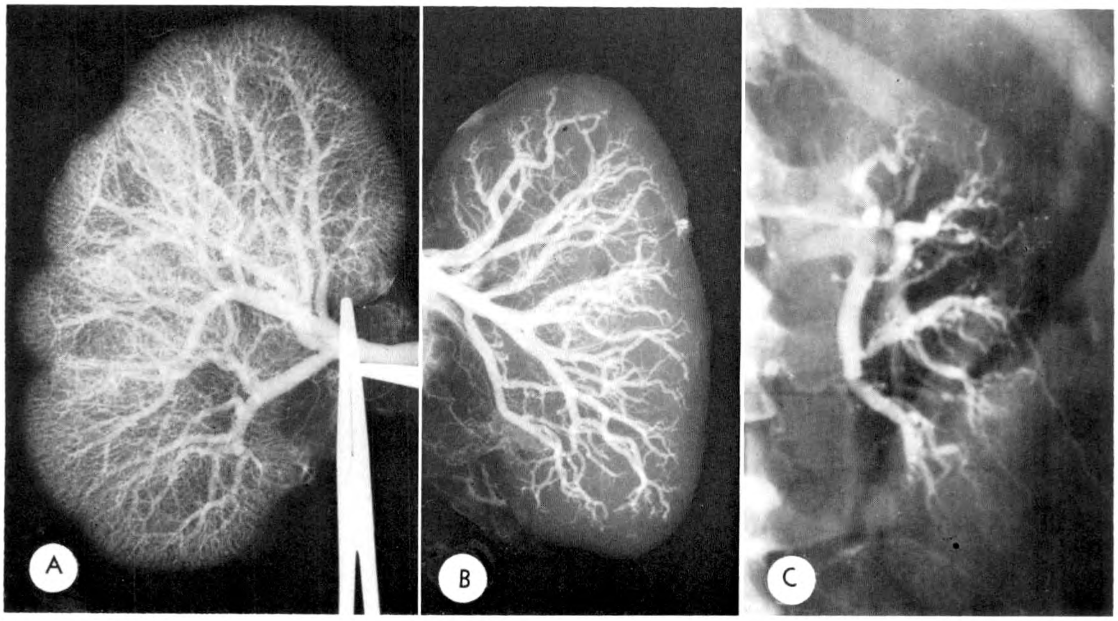


FIG. 5. Malignant nephrosclerosis. (*A*) Postmortem arterial injection of normal kidney. Observe uniformity of vessel outlines and filling of small cortical branches. (*B*) Postmortem arteriogram of malignant nephrosclerosis. The kidney is contracted and the small intrarenal arteries end abruptly. The cortical vessels are markedly reduced in number. (*C*) Selective arteriogram of this patient shows that the essential features of the anatomic study are depicted *in vivo.*

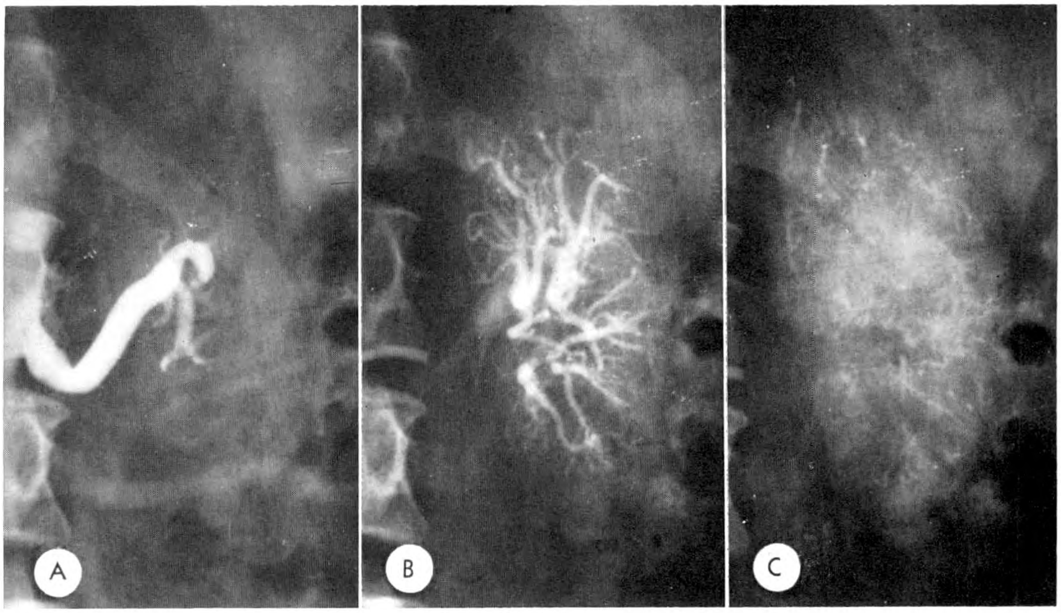


Fig. 6. Malignant nephrosclerosis. (*A*) The main renal artery is large. (*B*) The intrarenal branches have a gnarled appearance and are shortened abruptly with distal pruning. (*C*) The nephrogram is faint and the kidney contracted.

their significance is well known. A discussion of these lesions is not the subject of this paper. It should be emphasized, however, that in the presence of an obstructive lesion of the main artery every attempt should be made to visualize the finer arterial branches distally and evaluate the arterial run-off. Pathologic changes in the small arteries beyond a stenotic lesion or in the opposite kidney may explain unsatisfactory results following surgical correction of main artery obstruction in some patients.

In this regard the following 2 cases are of interest:

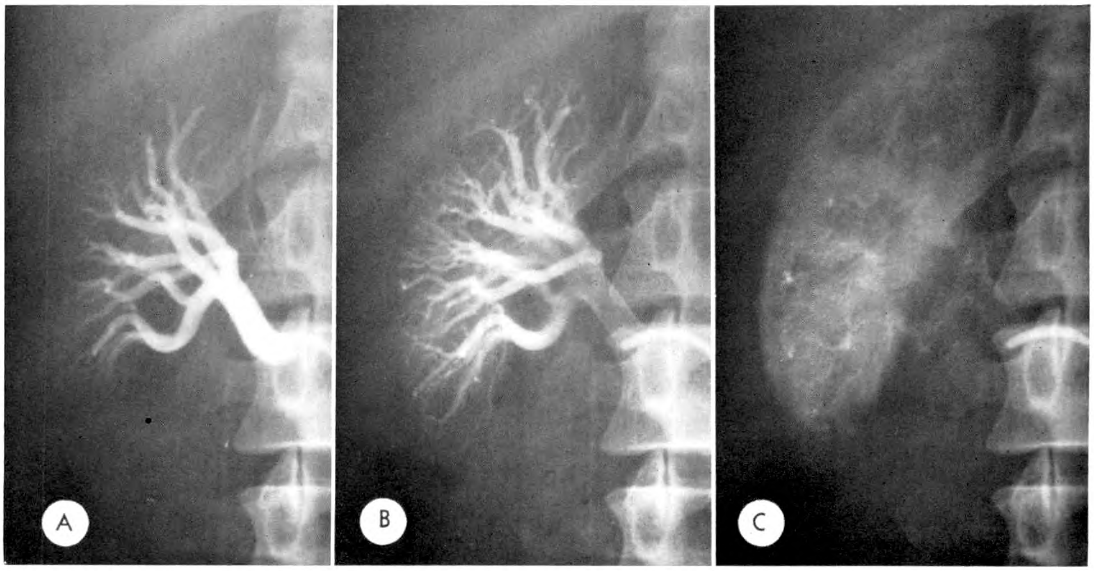


Fig. 7. Malignant nephrosclerosis. (*A*) Large main renal artery and primary branches are dilated and terminate abruptly. (*B*) The vascular tree is shortened. (*C*) Faint nephrogram with reduced renal mass.

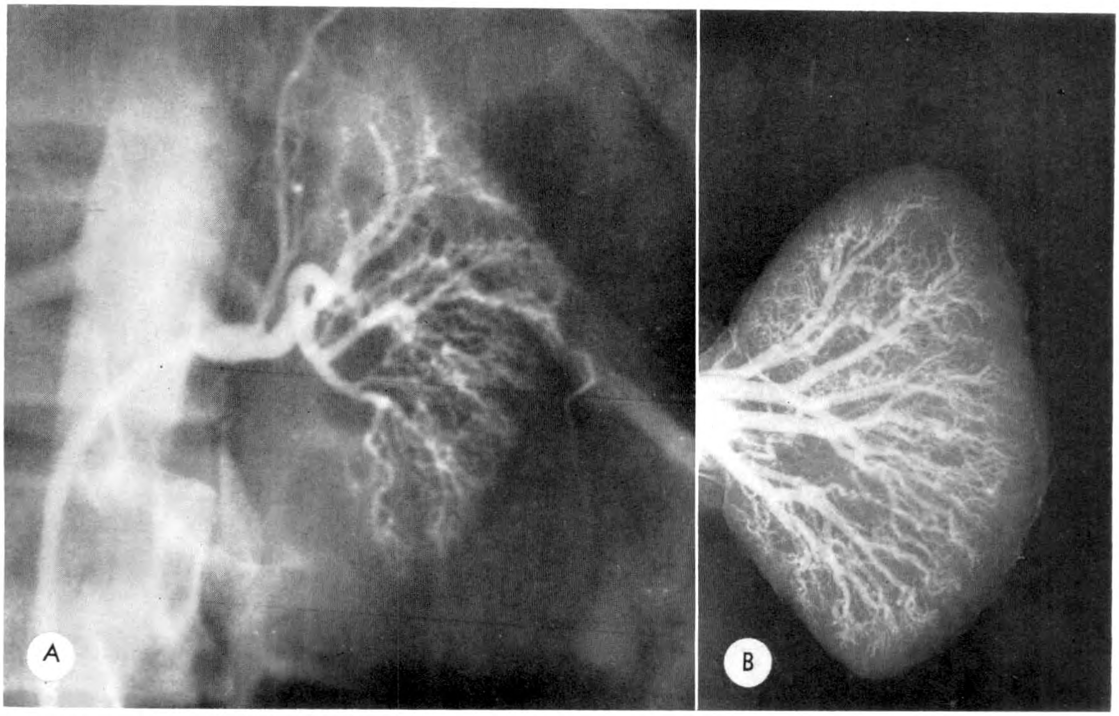


Fig. 8. Chronic glomerulonephritis and malignant hypertension. (*A*) Selective arteriogram of 18 year old girl shortly before death. There is marked contraction of the kidney with loss of the finer vascularity. (*B*) Postmortem renal arteriogram reveals almost complete absence of filling of cortical vessels.

Case 1. A 50 year old Negro female with severe hypertension was studied with a mercury 203 renoscan which revealed bilateral reduction of functioning renal tubular mass. On renal arteriograms the left kidney appeared larger than the right in spite of a main artery stenosis on the left side. The main artery to the right kidney was normal. The atherosclerotic lesion on the left side was removed by endarterectomy. The severe hypertension that persisted after surgery was not surprising when the extent of the nodular obstructive lesions in the smaller arteries of the right kidney was appreciated by careful study of the arteriogram (Fig. 9, *A* and *B*).

Case 2. A 26 year old Negro male was admitted for evaluation of diastolic hypertension. Intravenous urograms revealed prompt bilateral excretion of contrast material in equal concentration. The kidneys were equal and normal in size (right 13 cm., left 12.5 cm.). Bilateral selective renal arteriograms (Fig. 10, *A* and *B*) showed a stenotic lesion near the origin of the right renal artery. The main renal artery on the left side was normal. Small vessel disease was present bilaterally, but was clearly less evident in the right kidney which was supplied by the stenotic renal artery. The mercury renoscan (Fig. 10 *C*) on two occasions disclosed a normal scan on the right with good uptake. The functioning left renal mass was considerably smaller than the right with an irregular uptake. Although pathologic data are lacking, this case is probably an example of unequal development of bilateral obliterative intrarenal vascular disease suggesting unilateral renal disease by function studies.

These cases are in accord with experimental observations in animals by Wilson and Byrom[33,34] that the kidney supplied by the stenotic renal artery was "protected" from the vascular lesions of high blood pressure. The authors stress the fact that the kidney on the side of arterial occlusion was potentially the healthier one and, if possible, should be preserved.

2. *Lesions of Segmental Arteries.* Segmental renal artery stenosis may not be de-

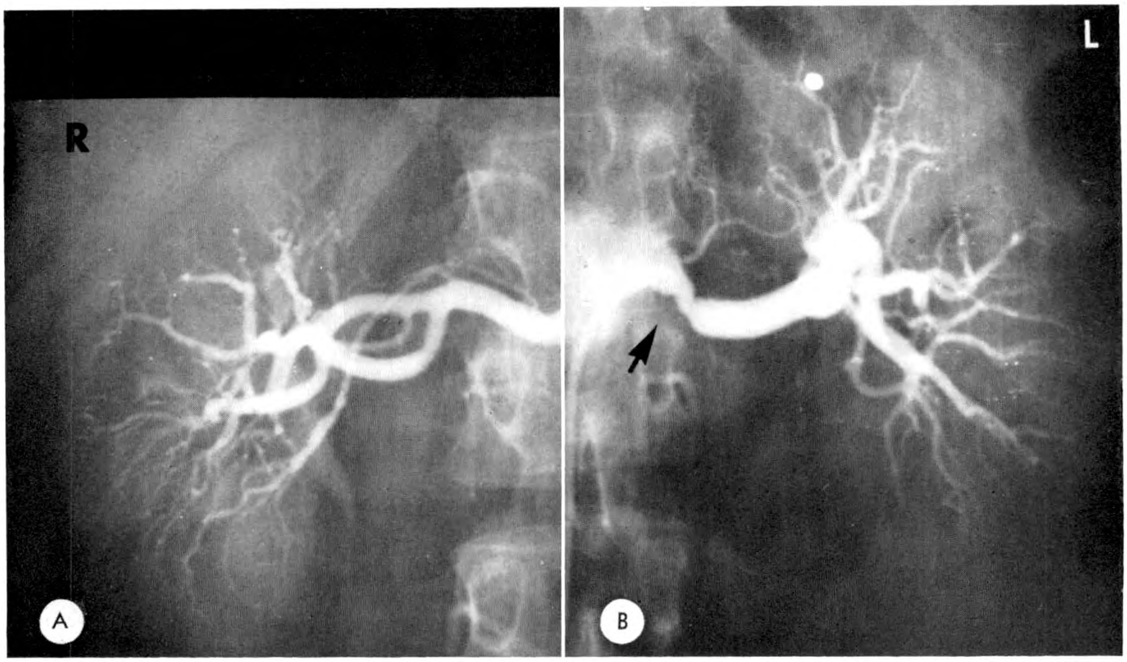


FIG. 9. Case 1. (*A*) The main renal artery is normal. Small vessel changes of nephrosclerosis are present. (*B*) Left kidney. A stenotic lesion of the main artery (arrow) is seen and small vessel disease is less marked than in opposite kidney. Severe hypertension persisted after left endarterectomy.

tected by abdominal aortography due to inadequate visualization of the segmental branches and intrarenal vessels.[10] Selective arteriography has proved valuable in the diagnosis of segmental artery occlusion (Fig. 11, *A*, *B* and *C*). It is of interest that in this patient with segmental renal infarction there was complete nonfunction of the involved kidney as determined by intravenous urography and mercury scanning at the time of acute flank pain (Fig. 11, *D* and *E*). Selective arteriography provided an immediate, otherwise unobtainable, diagnosis.

C. PYELONEPHRITIS

1. *Acute Pyelonephritis.* Our arteriographic experience in this condition is very limited. In one patient the involved kidney was swollen and increased in size. The segmental and interlobar arteries were spread, elongated and separated from each other.

2. *Chronic Pyelonephritis.* This disease has been studied in our department both by selective renal arteriography and postmortem arterial injections of kidneys of patients dying from this disease. The selective arteriogram shows a reduced diameter of the main renal artery proportional to the reduced functional renal mass. The interlobar arteries are crowded in the diminished renal volume, and there is tortuosity of interlobar and arcuate vessels which may be severe. In some instances, localized areas of reduced vascularity are present.

The nephrographic and venous phases provide further information for the over-all evaluation. The periphery of the kidney reveals gross indentations due to cortical scarring. The nephrogram is disproportionately dense, a result of crowding of vasculature due to loss of interstitial tissue. The renal veins paradoxically are visualized early.

Figure 12, *A* and *B* shows unilateral pyelonephritis with normal renal vasculature in the unaffected kidney and severe vascular changes in the diseased kidney. In Figure 13, the severe vascular crowding of

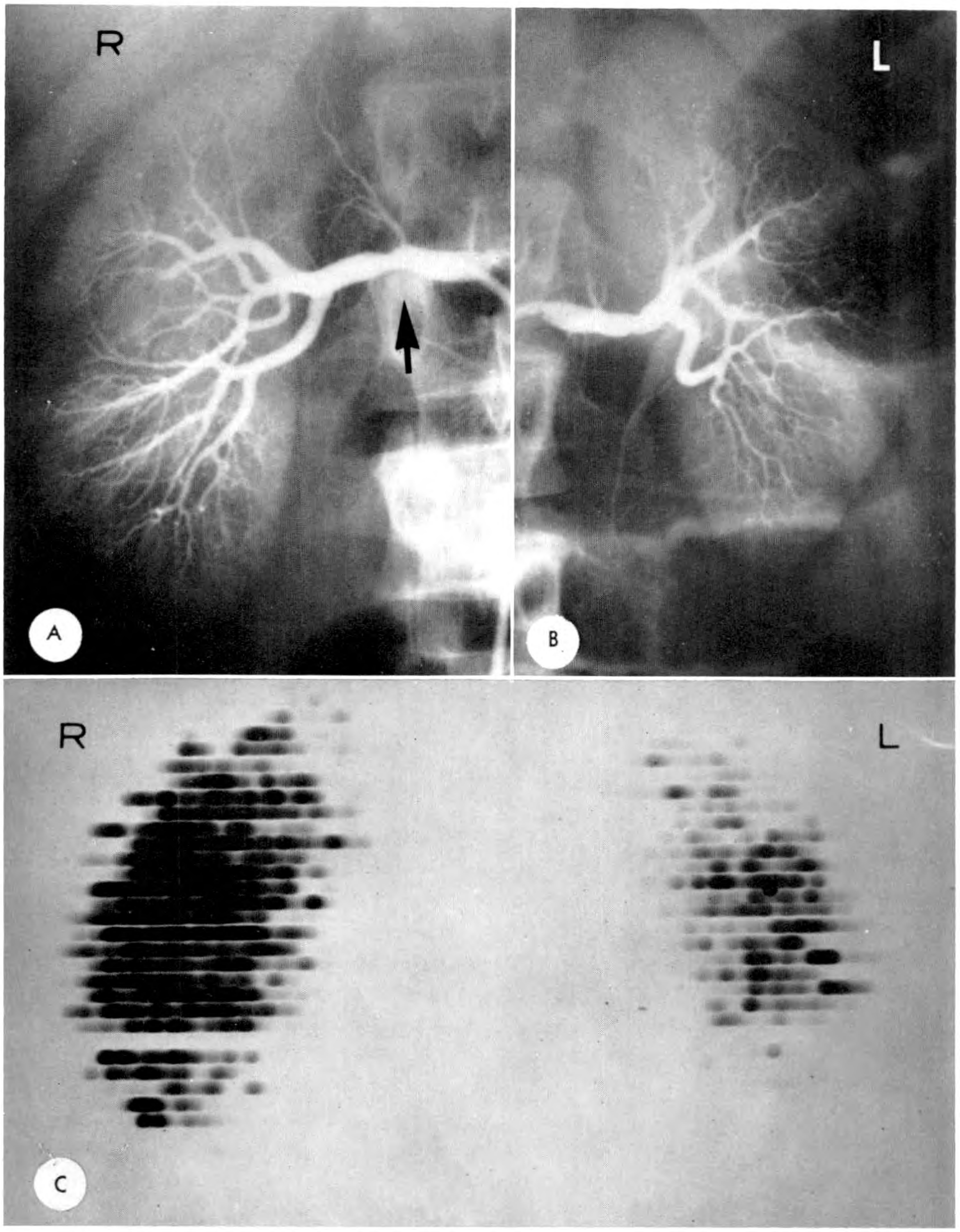


Fig. 10. Case 2. (*A*) Right kidney. Arrow points to stenotic lesion of main artery with moderate small vessel changes distally. (*B*) Left kidney. The main artery is normal, and there is severe narrowing of parenchymal arteries with wide angle bifurcations. (*C*) Renoscan. The functioning left renal mass is smaller than the right with an irregular uptake. This case is probably an example of unequal development of bilateral obliterative intrarenal vascular disease suggesting unilateral disease by function studies.

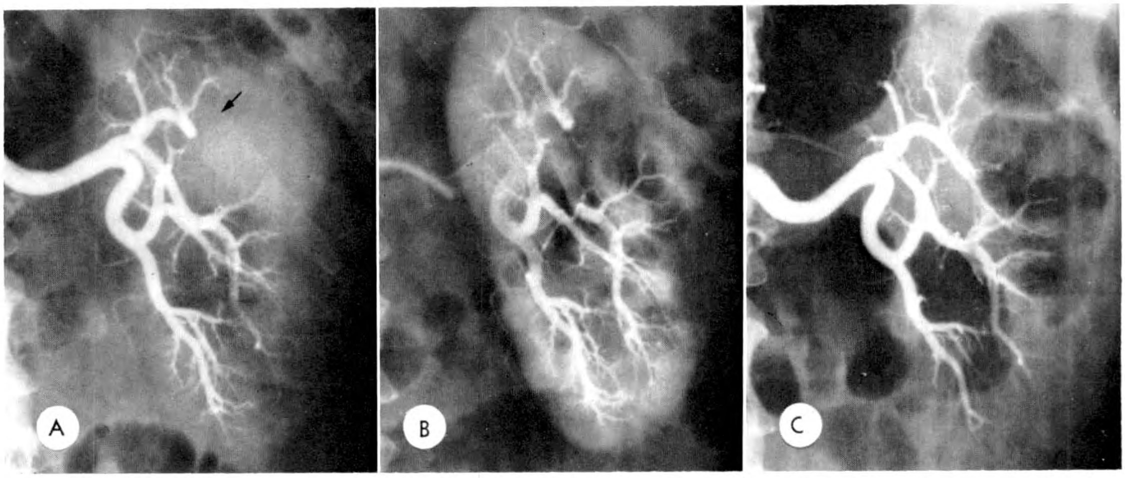


FIG. 11. Segmental renal artery occlusion. (*A*) Segmental artery (arrow) ends abruptly. (*B*) Avascular parenchymal defect present on the nephrogram. (*C*) Repeat arteriogram 12 days following acute flank pain reveals partial filling of occluded artery. (Reproduced with permission of *Journal of Urology*.)

end stage disease is evident. Figure 14, *A*, *B* and *C* shows some of the changes in chronic pyelonephritis. The nephrogram reveals dense cortical indentations with minimal arterial abnormalities.

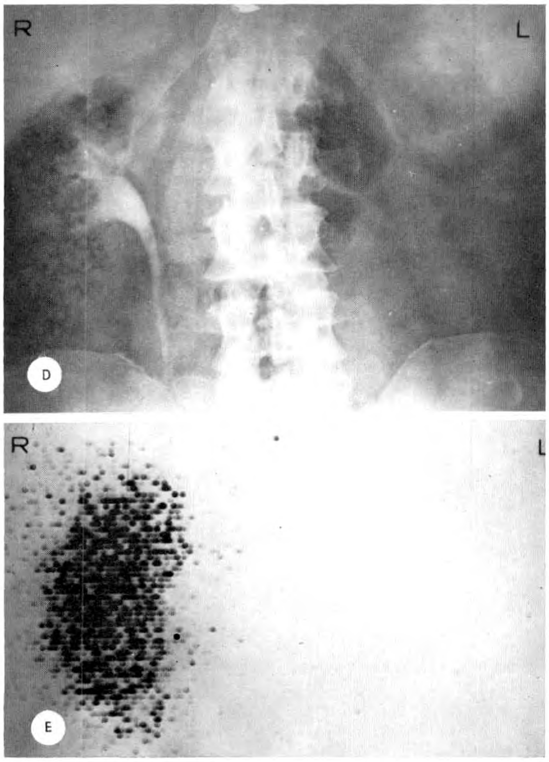


FIG. 11. (*D*) Intravenous urogram and (*E*) mercury renoscan disclose complete nonfunction of left kidney at the time of initial arteriography.

It is noteworthy that in experimental pyelonephritis in animals[17] postmortem arteriograms show many similarities to our clinical observations.

D. HYDRONEPHROSIS

Hydronephrosis cannot be strictly classified as a nonsurgical condition. The arteriographic findings are presented here as they may be important in the differential diagnosis of certain medical diseases, particularly polycystic renal disease and tuberculosis.

The kidney with only acute or mild chronic obstruction of the collecting system presents a normal arteriogram and nephrogram. With longstanding obstruction and distention of the renal pelvis, the interlobar and arcuate arteries become stretched and attenuated over the distended sac, with eventual disappearance of the finer branches by pressure atrophy. Figure 15, *A* and *B* demonstrates these changes in a small nonfunctional hydronephrotic sac. In such patients selective arteriography may indicate the volume of functioning parenchyma present.

E. TUBERCULOSIS

In tuberculosis of the kidney, the arteriogram reveals one of several patterns. When

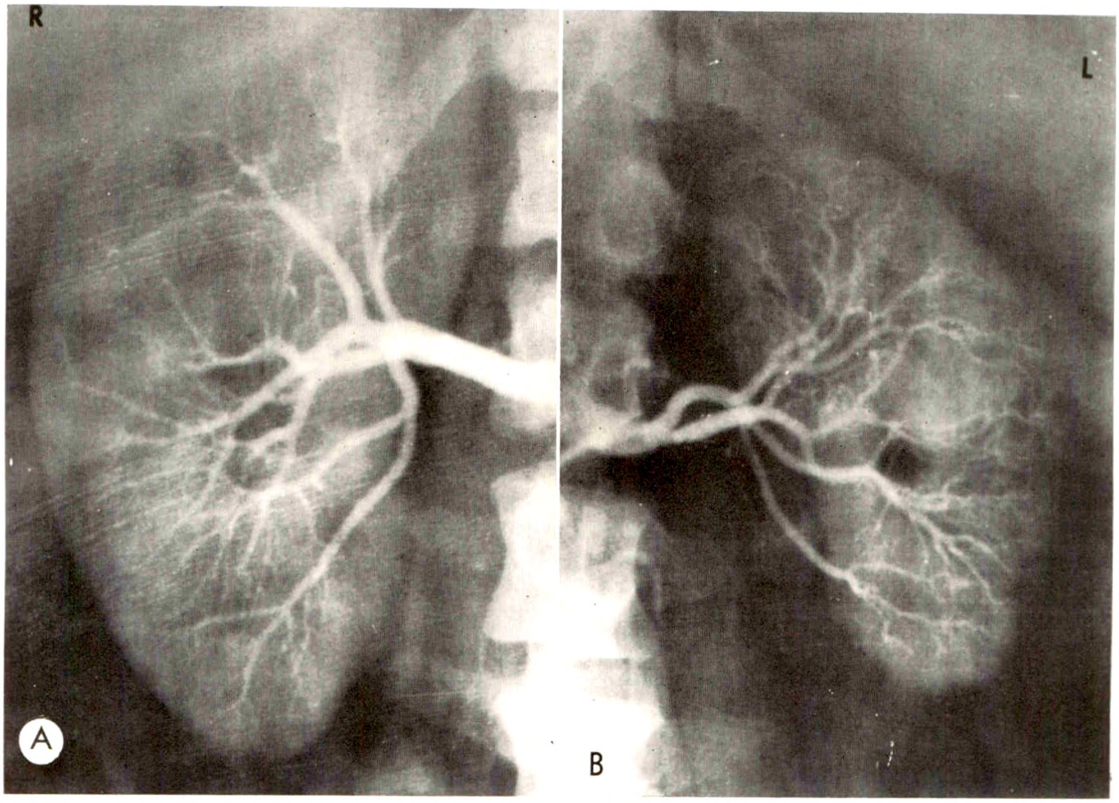


FIG. 12. Unilateral chronic pyelonephritis. (*A*) Right kidney shows normal vasculature. (*B*) Severe tortuosity of interlobar and arcuate arteries in moderately contracted kidney.

only small tuberculous foci are present, a normal arteriographic pattern is noted. More extensive parenchymal disease with loss of tissue produces a tortuous, beaded appearance of the interlobar arteries similar to that seen in nontuberculous pyelonephritis (Fig. 16, *A* and *B*). When tuberculous destruction is marked with calyceal necrosis and cavity formation (caseocavernous tuberculosis), elongated, thin arteries may be seen to course around abscess cavities with irregular filling defects in the nephrogram (Fig. 17, *A* and *B*). If renal tuberculosis manifests itself as a large granuloma, it may assume the characteristics of a nonmalignant mass lesion.[31]

Our findings in renal tuberculosis have been similar to those reported by Frimann-Dahl.[11]

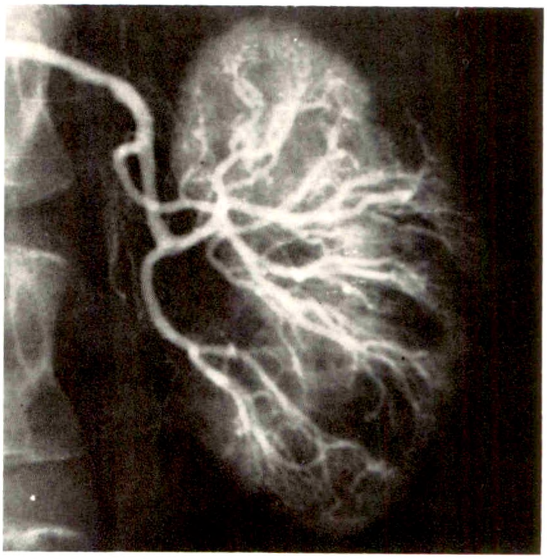


FIG. 13. Chronic pyelonephritis. End stage pyelonephritis with severe vascular crowding in atrophic renal mass.

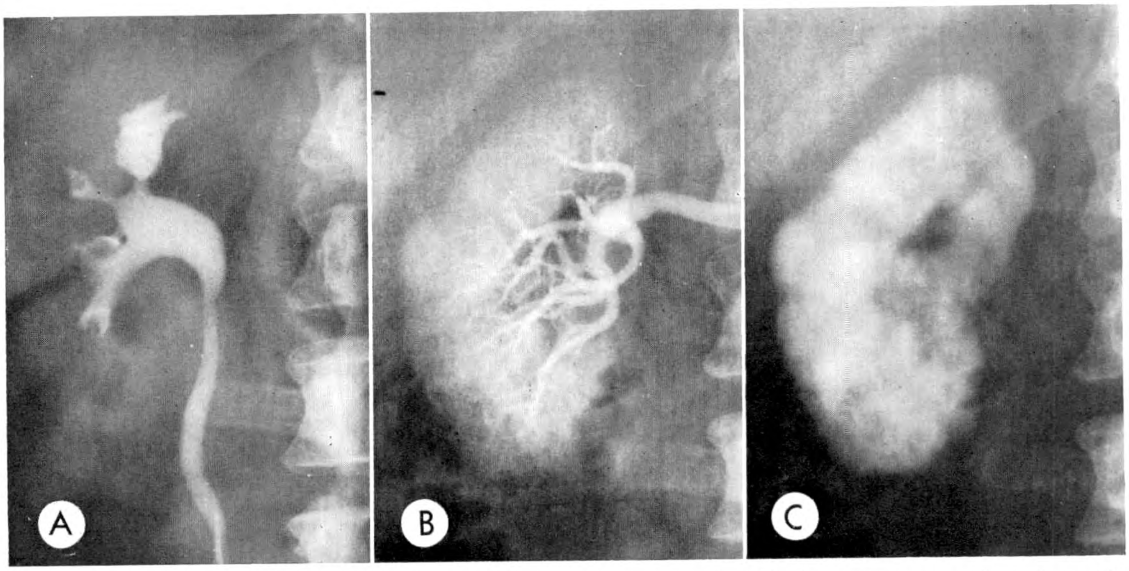


Fig. 14. Chronic pyelonephritis. (*A*) Retrograde pyelogram reveals widening of upper pole calyx. (*B*) Arteriogram discloses irregular contour with tortuosity of small intrarenal arteries. There is reduced vascularity in upper portion of kidney. (*C*) Nephrogram is dense with well defined cortical scarring.

F. POLYCYSTIC RENAL DISEASE

We have studied this disease only in adult patients. The arteriographic appearance of this condition is dependent upon the size and number of cysts present. When the kidneys are full of small tightly packed cysts, the arteriogram reveals elongated thin arteries without visible normal renal tissue, and the nephrogram shows multiple cystic areas of rarefaction (Fig. 18, *A* and *B*). In other instances, the kidneys are only partially replaced by cysts, some of which are quite large, and the arteriogram suggests the presence of multiple large simple

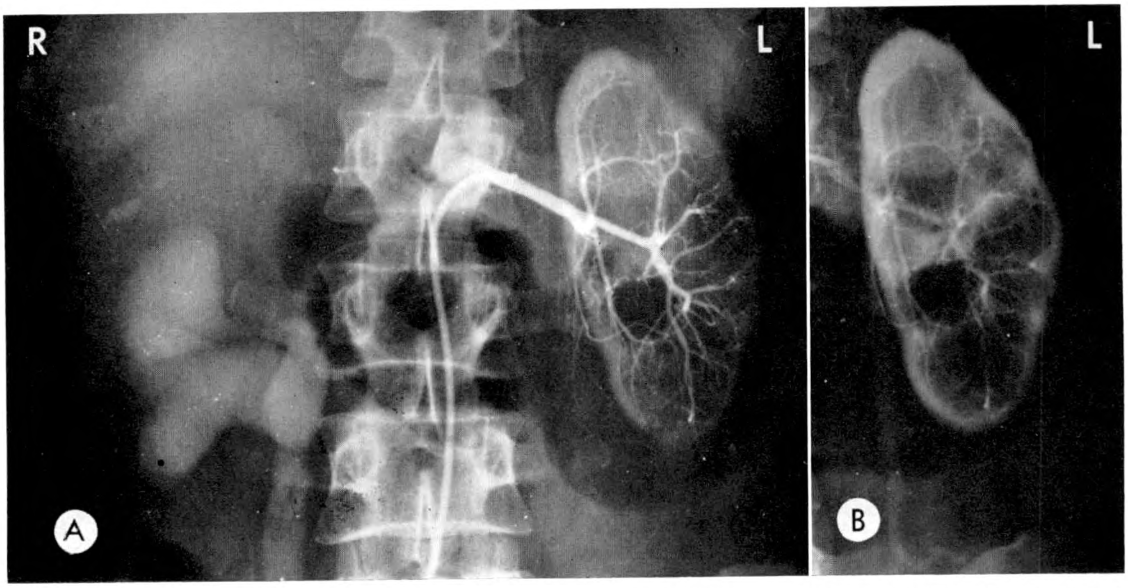


Fig. 15. Hydronephrosis. (*A*) Intravenous urogram and left arteriogram. Right pelvicalyceal system and ureter dilated. Arteriogram shows spread of interlobar arteries with loss of finer branches. (*B*) Nephrogram reveals only shell of functioning parenchyma present.

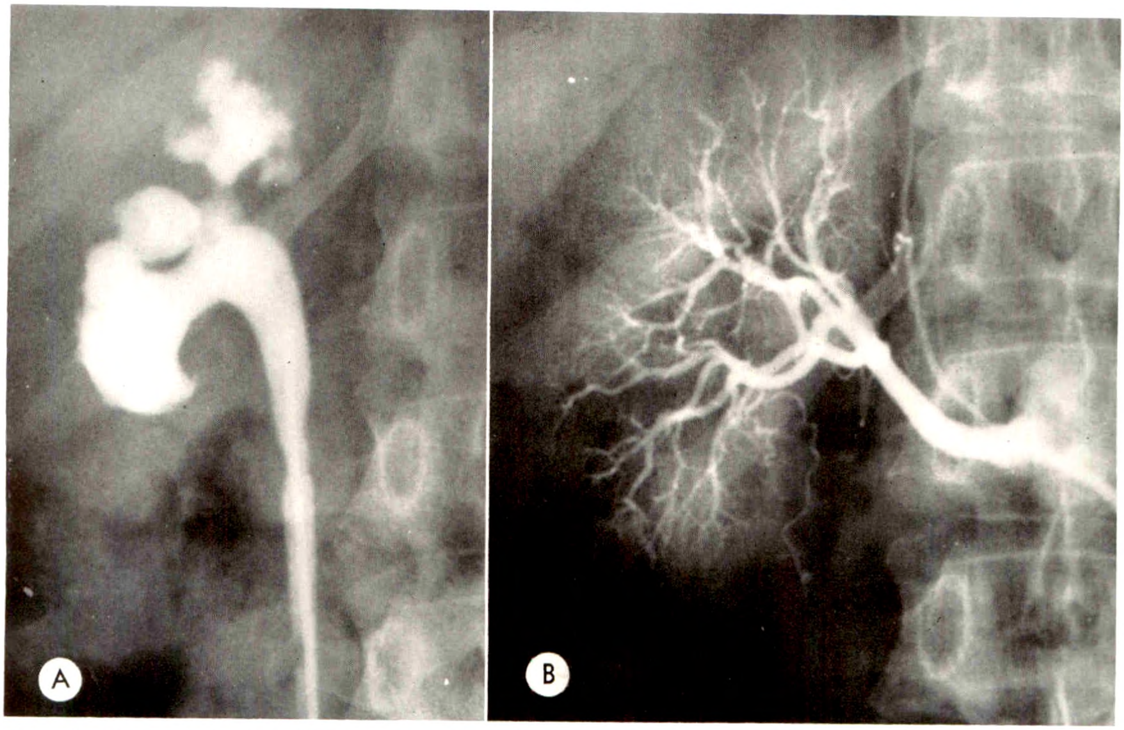


Fig. 16. Tuberculosis. (*A*) Right retrograde pyelogram. Dilatation of collecting system with marked irregularity of upper group of calyces. (*B*) Selective arteriogram discloses vascular changes resembling those of chronic pyelonephritis.

cysts separated by normal renal parenchyma. We have studied one patient in whom the condition was unilateral (Fig. 19, *A*, *B* and *C*). In another patient with renal failure and severe hypertension, there was complete replacement of the right kidney by cysts (Fig. 20, *A* and *B*). The left kidney revealed at least one large cyst in the upper pole and the effects of hypertension were present in the small intrarenal arteries (Fig. 20 *C*).

G. UNILATERAL RENAL VEIN THROMBOSIS

One relatively rare etiologic possibility of the nephrotic syndrome is bilateral renal vein thrombosis. Unilateral renal vein thrombosis is an even rarer cause of this syndrome.[23] In one such patient studied by selective renal venography and arteriography, the arteriogram disclosed straightened and spread intrarenal vessels in keeping with generalized swelling of the kidney. This case will be the subject of a separate report.

DISCUSSION

The value of selective renal arteriography in the differential diagnosis of neoplasms and cysts of the kidney has been well established.[3,8]

It is in the evaluation of patients with hypertension that selective arteriography may ultimately prove to have its greatest application. Considerably more information is needed for the proper selection of hypertensive patients who are most likely to benefit from surgical repair of renovascular lesions. Conceivably, selective arteriography with careful attention to the status of the small intrarenal vessels may offer valuable clues in the preoperative evaluation. At present, we feel that selective arteriography should be employed in all cases in which surgery for the treatment of hypertension is contemplated.

In the diagnosis of pyelonephritis, selective renal arteriography has proved to be of considerable value. Frequently, the

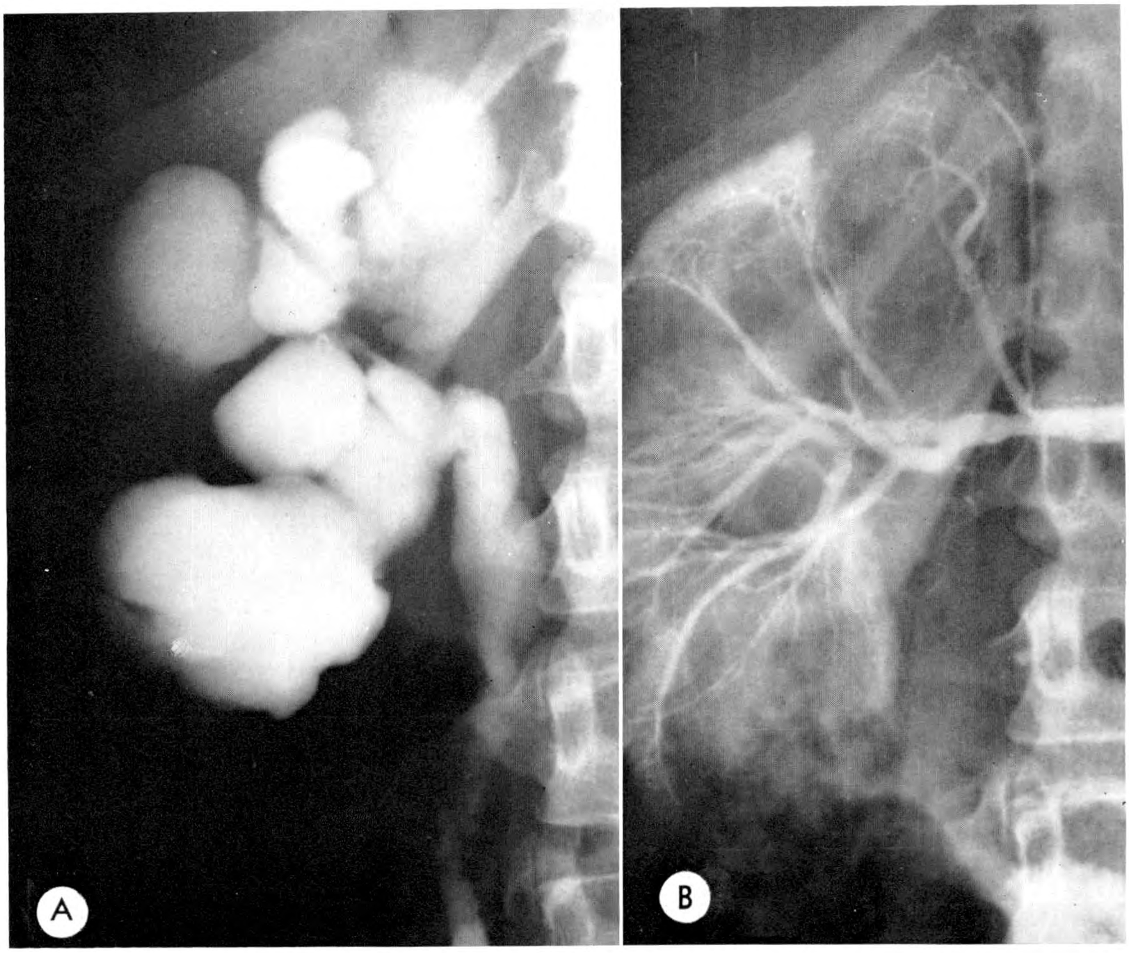


Fig. 17. Tuberculosis. (*A*) Right retrograde pyelogram. Severe dilatation of calyces which are partially eroded. Marked involvement of ureter with irregular areas of dilatation and constriction. (*B*) Arteriogram shows attenuated arteries coursing around large cavities in renal parenchyma.

survey roentgenograms of the abdomen and intravenous urograms provide only limited information in patients with this condition. Pyelographic changes result from scarring of the parenchyma, and it is often not possible to distinguish an inflammatory or vascular origin on the basis of pyelographic deformities. The results of our studies suggest that, of the available radiographic techniques, selective arteriography more clearly defines the nature and extent of the parenchymal changes and may also differentiate segmental from diffuse disease.

Selective renal arteriography may aid in the differential diagnosis of the unilateral small kidney. The principal conditions responsible for this entity are atrophic pyelonephritis, renal artery stenosis and congenital hypoplasia.[24] If the arteriogram depicts an essentially normal vascular pattern, the diagnosis of true congenital hypoplasia appears justified.

The majority of our cases have been patients with disease processes that result in reduction of renal size and apparent shortening of the parenchymal vessels. However, some renal diseases are characterized by an increase in the size of the kidney. In these cases the segmental and parenchymal arteries are thinned and elongated with uniform caliber. Acute pyelonephritis, polycystic disease, renal vein thrombosis, and some cases of hydronephrosis and tuberculosis have produced this type of renal arterial change.

Many other diseases are manifest by changes in the renal arteries. Polyarteritis nodosa generally involves the large arteries with distal infarction.[27] In this condition, a large number of small aneurysms of the medium- and small-sized arteries of the kidney may be demonstrated.[21] Scleroderma of the kidney affects the small interlobular arteries with a subintimal infiltrative lesion.[27] Disseminated lupus and primary amyloidosis, to name a few, are other diseases that involve the renal vessels.[32] We have not had an opportunity to study patients with these conditions by arteriography.

Although selective renal arteriography has made it possible to uncover small vessel alterations in various renal disorders, much remains to be learned about the life history of these changes. Selective renal arteriography may prove to be a useful method by which to find out whether these pathologic changes can be influenced by therapeutic measures.

Also, in order to determine more precisely the significance of small vessel changes in the evaluation and prognosis of individual renal diseases, a much more extensive correlation of arteriographic, clinical and pathologic data is necessary. Studies of this type are now being conducted in this department in an effort to obtain a better understanding of the fundamental pathologic processes involved.

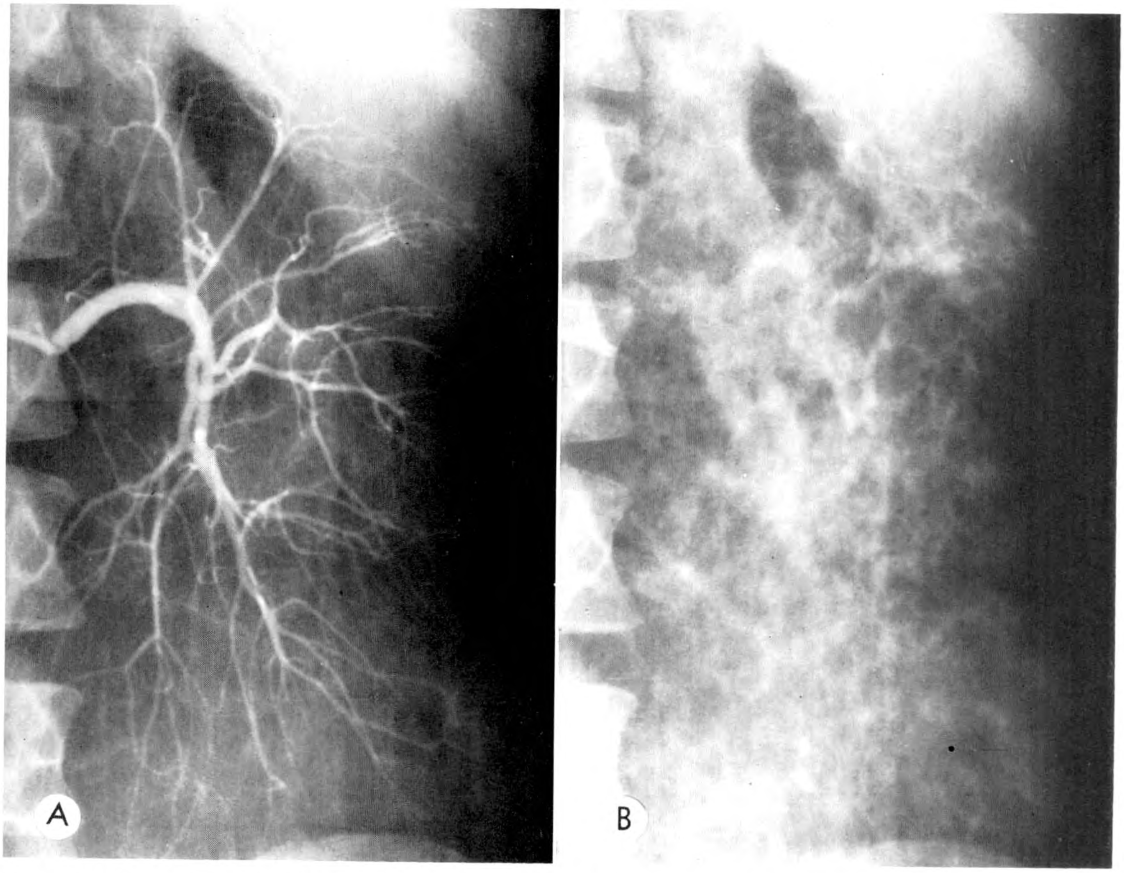


Fig. 18. Polycystic disease. (*A*) Arteriogram reveals a markedly enlarged kidney with thin elongated arteries. (*B*) Multiple areas of cystic rarefaction are visible in the nephrogram. (Reproduced with permission of *Journal of Urology*.)

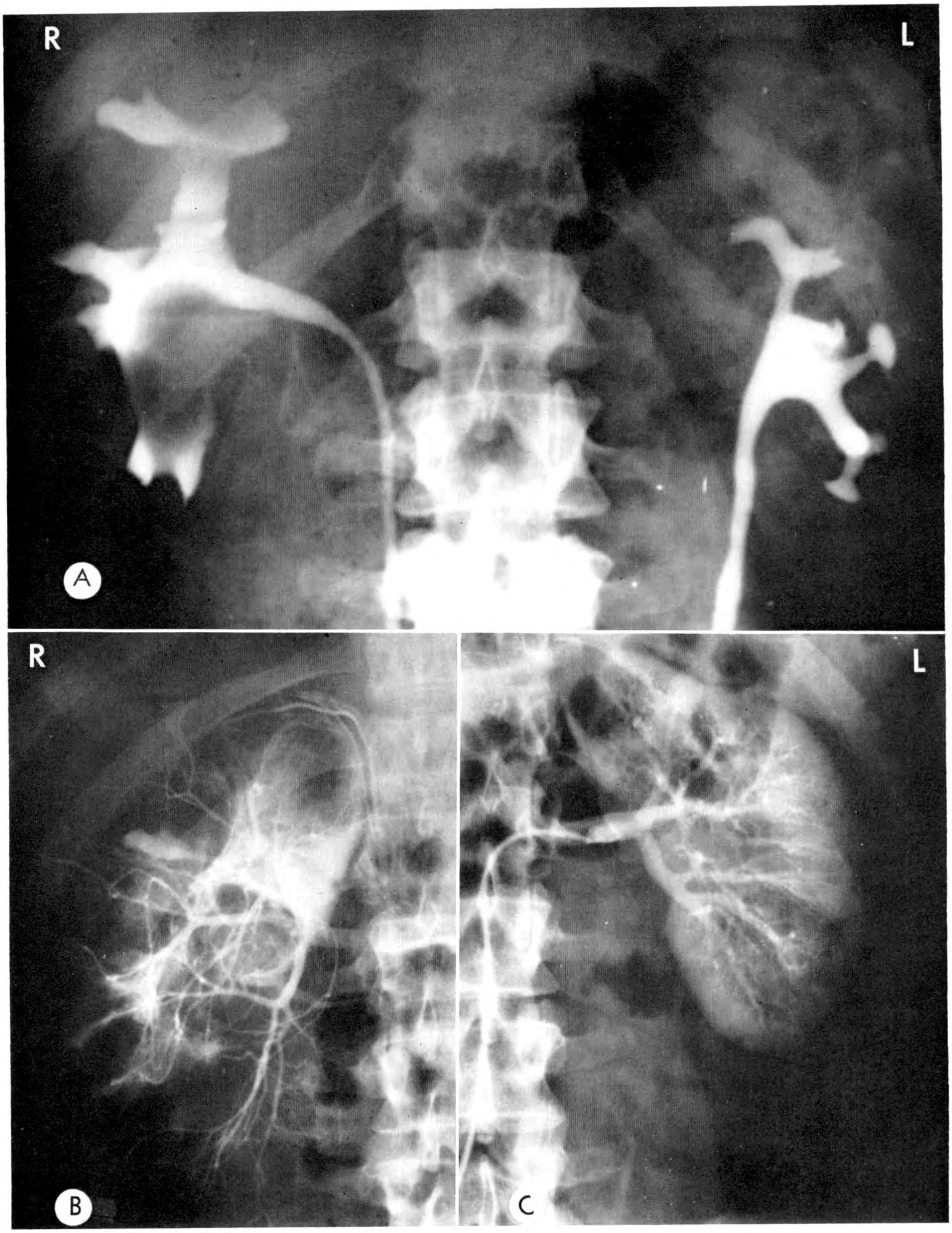


Fig. 19. Unilateral polycystic disease. (*A*) Retrograde pyelogram shows marked enlargement and deformity of right collecting system and normal left side. (*B*) Arteriogram of right kidney discloses multiple large and small irregular radiolucent filling defects in renal parenchyma with deformity of the intrarenal arteries. (*C*) Left kidney. Arteriogram normal.

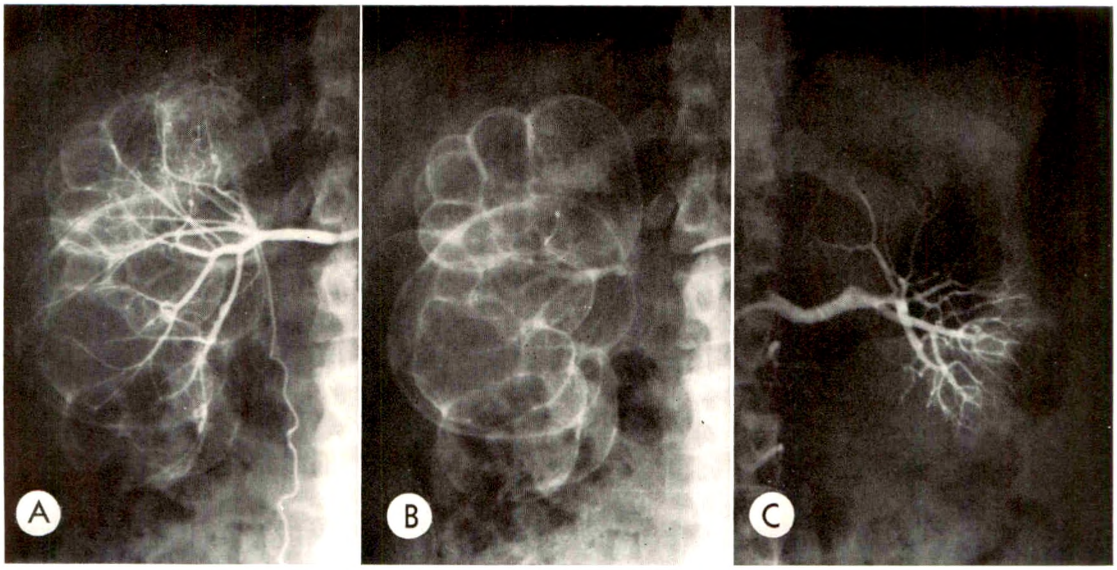


Fig. 20. Polycystic disease, hypertension and renal failure. (*A*) Right arteriogram. The renal vasculature is thinned and stretched. (*B*) Nephrogram. Only shell of cortex covers multiple cystic cavities. (*C*) Arteriogram of left kidney. A large cyst is present in the upper pole and small vessel changes are consistent with hypertension.

SUMMARY

1. Selective renal arteriography permits visualization of the small intrarenal arteries to a degree approaching that obtained by opaque injection of anatomic specimens.

2. The arteriographic features of benign and malignant hypertensive vascular disease, segmental arterial occlusion, pyelonephritis, hydronephrosis, tuberculosis, polycystic renal disease and unilateral renal vein thrombosis have been described.

3. Emphasis has been placed on small vessel changes rather than main artery lesions in these disease entities. In some patients with occlusive disease of the main renal arteries, the status of the small intrarenal vessels may be of considerable importance.

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RADIOLOGIC EVALUATION OF ACUTE RENAL INFARCTION*

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IN A general hospital, a small fraction of cases of abdominal pain will be encountered due to renal infarction following renal arterial occlusion.[2,5] It is important that the source of the pain be recognized early, not only to save the patient a lengthy, costly work-up as the etiology is sought, but also to ensure that there is time for possible surgical intervention to save the affected kidney if the occlusion is in the main renal artery. Roentgenographic examinations, such as intravenous pyelography and renal angiography, play a significant role in establishing the correct diagnosis.[1] It is with this aspect of these cases that the present paper is primarily concerned.

CLINICAL MATERIAL

This study is based upon a series of 12 cases seen at the Massachusetts General Hospital since 1955. In each of these patients an underlying disease was present. Nine of them had heart disease (4 rheumatic, 4 old myocardial infarction, and 1 adult fibroelastosis). Two patients had undergone recent surgery: 1 splenectomy for idiopathic thrombocytopenic purpura, and 1 renal artery repair for fibromuscular hyperplasia. The remaining patient had suffered recent severe external trauma. Cardiac arrhythmias were frequent, while history of past embolization was elicited 4 times.

Pain was the usual presenting symptom. It varied in degree from slight to moderate and was entirely nonspecific in nature. In 9 of the cases, the pain was principally in the costovertebral angle. Systemic symptoms such as fever, nausea, or vomiting were unusual and insignificant. Urinary tract symptoms, including frequency and urgency, were not noted.

Laboratory values were of limited usefulness. The only positive blood cell value was the white blood cell count which was always over 11,000. Urinalysis was abnormal in all cases in which it was performed. Gross hematuria did *not* occur, although several red blood cells were usually seen microscopically. An equally significant urinary finding was albuminuria, which was 1+ in 2 cases, 2+ in 3 cases, 3+ in 3 cases, and 4+ in 2 cases. The clinical and laboratory aspects of the cases are summarized in Table I.

REPRESENTATIVE CASES

Five cases have been selected as representative of our observations. The roentgen findings in each are described and the general radiologic features of the series are subsequently discussed.

Case I. E.E., a 74 year old white female, was admitted to the hospital because of lower abdominal crampy pain. The pain soon spread to the left flank and was accompanied by slight nausea and vomiting. There were no urinary tract symptoms.

The patient had sustained a myocardial infarction 8 months prior to admission. Pertinent physical findings consisted of left costovertebral angle tenderness, atrial fibrillation with a pulse of 66, blood pressure of 190/80, and a temperature of 99.8° F. The leukocyte count was 20,900. Urinalysis revealed a specific gravity of 1.019, 1+ albuminuria, and no cells.

Roentgenographic Findings.

Intravenous Pyelography. The plain roentgenogram of the abdomen revealed a moderate degree of ileus with normal psoas shadows and kidneys. Contrast material outlined a normal right upper collecting system and ureter. There was no function on the left (Fig. 1).

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TABLE I

CLINICAL AND LABORATORY FINDINGS IN 12 CASES OF ACUTE ARTERIAL RENAL INFARCTION

Case No.	Age and Sex	Predisposing Disease	Other Embolization	Pain	Systemic Symptoms	White Blood Cell Count	Urinary Findings		
							Specific Gravity	Urine Albumin	Red Blood Cells
I	74 F	Old myocardial infarct	—	Lower abdomen and left flank	Slight nausea and vomitings	20,900	1.019	1+	0–2
II	72 F	Rheumatic heart disease	1. Right middle cerebral artery 2. Aortic bifurcation 3. Right femoral artery	Right lower and upper quadrant	Slight nausea and vomitings	26,000	1.016	2+	Occasional
III	57 M	Rheumatic heart disease	Left femoral artery	Left costovertebral angle	No	15,000	1.015	3+	Occasional
IV	68 F	Old myocardial infarct	—	Left costovertebral angle	No	—	1.015	3+	10–12
V	43 M	Fibroelastosis	—	Right costovertebral angle	Vomited twice; temperature 102°F.	17,000	1.006	4+	4–6
VI	44 M	Rheumatic heart disease	—	Left costovertebral angle	No	17,000	1.025	4+	Many
VII	68 F	Rheumatic heart disease	Left middle cerebral artery	Right costovertebral angle	No	11,300	1.026	3+	0–2
VIII	57 F	Old myocardial infarct	—	Left costovertebral angle	Temperature 102°F.	16,400	1.010	1+	0–2
IX	75 F	Old myocardial infarct	Right ophthalmic artery	Left costovertebral angle	No	26,800	—	2+	0–2
X	19 F	Repair of fibromuscular hyperplasia	—	No	No	—	—	—	—
XI	42 F	Surgery and idiopathic thrombocytopenic purpura	—	Right costovertebral angle	Slight nausea	36,900	1.008	2+	Few
XII	13 M	Trauma	—	Generalized in abdomen	No	—	—	—	—

Retrograde Pyelography. The left collecting system and ureter were opacified and appeared normal (Fig. 2).

Renal Angiography. Aortography was performed by the Seldinger technique. The right main renal artery and branches were normal, but the left main renal artery was completely occluded just distal to its origin. No nephrogram appeared on the left (Fig. 3 and 4).

Comment. Nonfunction demonstrated on intravenous pyelograms with normal appearing calyces on retrograde pyelograms is a frequent finding. The arteriogram here revealed the block in the left main renal artery.

CASE II. C.D., a 72 year old white female, was admitted to the hospital because of nausea,

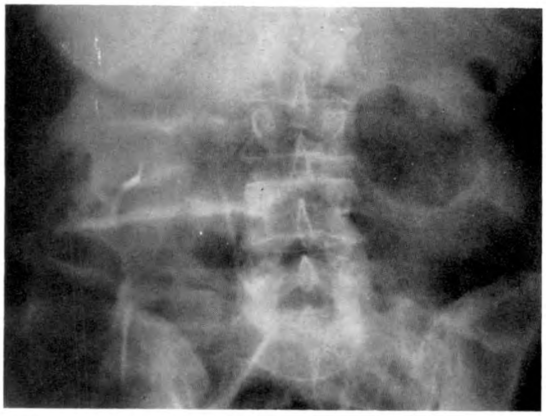

Fig. 1. Case 1. Intravenous pyelogram showing nonfunction on the left.

vomiting, and photophobia secondary to digitalis intoxication. Eight hours prior to admission, she had complained of the onset of pain in the right lower and upper quadrants of the abdomen. A diagnosis of rheumatic heart disease with mitral stenosis and regurgitation had been made 40 years previously. Three episodes of embolization had occurred in the past: (1) in 1952 an embolism of the right middle cerebral artery resulted in left hemiparesis; (2) in 1952 an aortic saddle embolus was successfully removed; (3) in 1959 a right femoral artery embolus was also removed. There was no history of urinary tract symptoms.

Pertinent physical findings included tenderness in the right flank and right upper and lower quadrants, mild congestive heart failure, atrial fibrillation with a pulse rate of 52, blood pressure of 160/90, and a temperature of 99.6° F. The leukocyte count was 26,000. Urinalysis revealed a specific gravity of 1.016, 2+ albuminuria, and an occasional red blood cell.

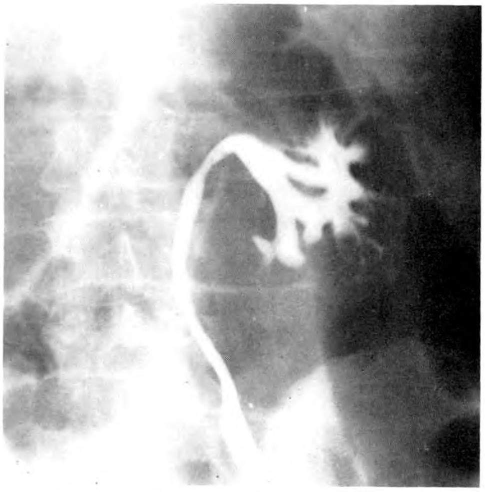

Fig. 2. Case 1. Retrograde pyelogram showing a normal upper collecting system on the left.

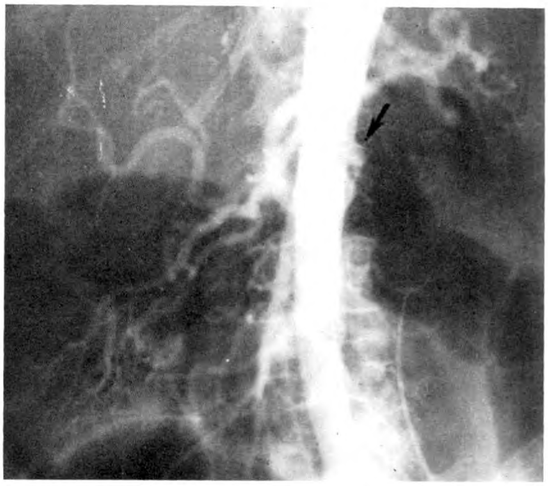

Fig. 3. Case 1. Renal angiogram showing complete occlusion of the left main renal artery (arrow).

Roentgenographic Findings.

Intravenous Pyelography. A preliminary roentgenogram of the abdomen revealed a moderate degree of ileus and obliteration of the right psoas shadow. The kidneys were of equal size, measuring 10.5×5 cm. Contrast material outlined a normal collecting system and ureter on the left. There was no function on the right (Fig. 5).

Renal Angiography. Aortography was performed by the Seldinger technique. The left main renal artery and the intrarenal branches were normal. There was an aberrant artery to the lower pole of the left kidney. On the right,

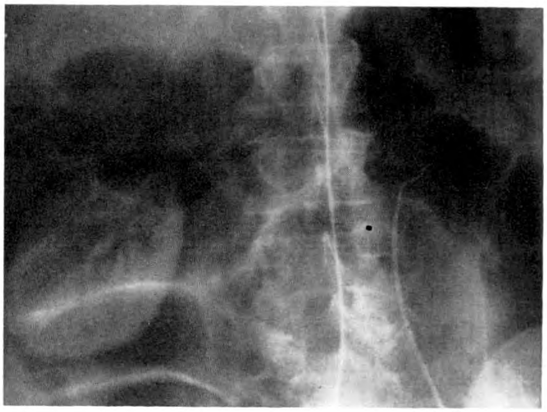

Fig. 4. Case 1. Absence of nephrogram on the left.

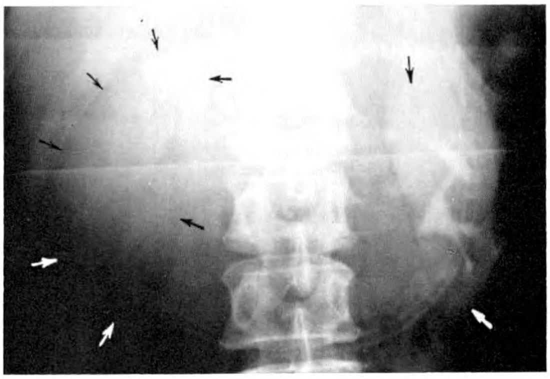

FIG. 5. Case II. Intravenous pyelogram showing nonfunction on the right. The right psoas shadow is poorly defined.

the main renal artery and larger segmental branches were normal. The smaller branches in the upper and lower pole areas were occluded, while the blood supply to the middle portion of the kidney was intact (Fig. 6 and 7). The flow of contrast material through the right kidney was delayed, with segmental branches still opacified, although at the same time there was a nephrographic effect on the left (Fig. 8). Roentgenograms obtained during the end phase showed a diminished nephrographic effect on the right as opposed to the normal left side (Fig. 9).

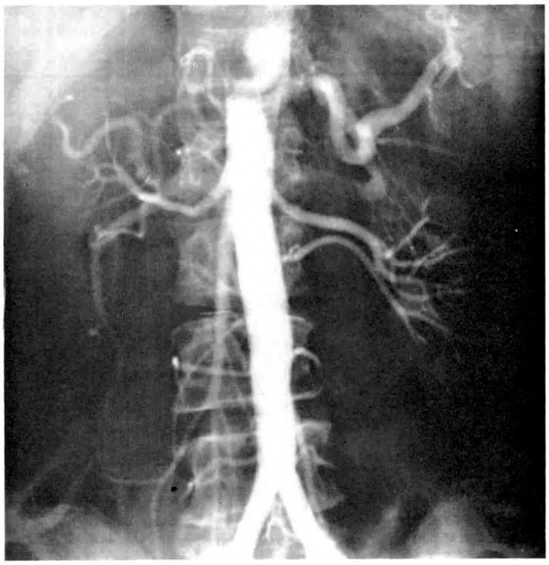

FIG. 6. Case II. Normal left renal angiogram demonstrating an aberrant artery to the lower pole. Normal right main renal artery and larger segmental branches. Smaller branches to the upper and lower poles are decreased.

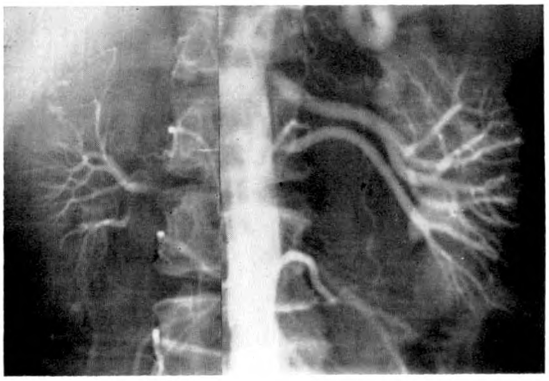

FIG. 7. Case II. Close-up of Figure 6 (composite illustration of the two sides).

Subsequent Course. Intravenous pyelography one month later revealed a smaller right kidney which measured 7.5 cm.×4 cm.; the left had not changed in size. Additionally, a moderate degree of function had returned on the right (Fig. 10).

Comment. Arteriography localized the site of embolization. Thirty days later the affected kidney had decreased in size by 3 cm.

CASE III. A.M., a 57 year old white male, was admitted to the hospital because of left flank pain of 5 hours' duration. Concomitant with the back pain, the patient had experienced pain in his left foot. A diagnosis of rheumatic heart disease with mitral stenosis and insufficiency had been made in the past. There was no history of nausea, vomiting, or urinary tract symptoms.

Pertinent physical findings included tender-

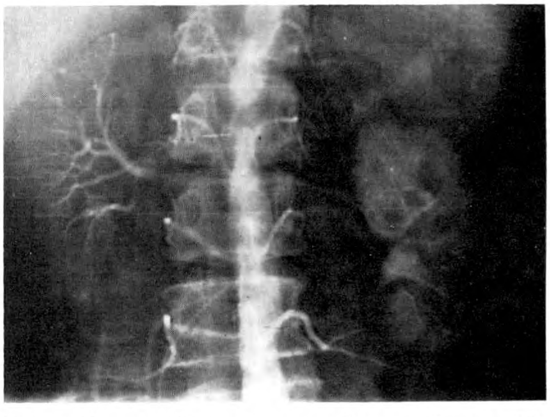

FIG. 8. Case II. Roentgenogram from nephrographic phase showing delayed circulation on the right.

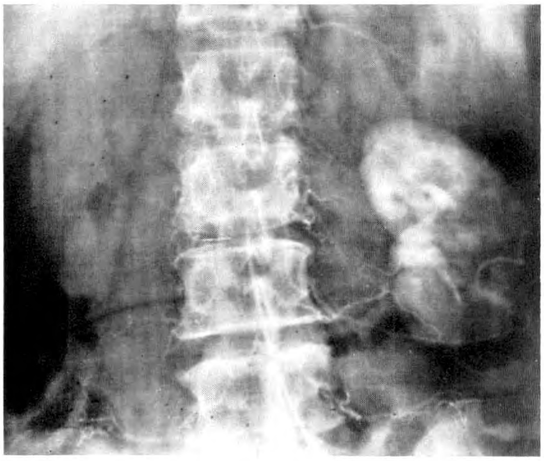

Fig. 9. Case II. Marked diminution of the nephrographic density on the right.

ness at the left costovertebral angle, absence of the left popliteal and foot pulses, mild congestive heart failure, atrial fibrillation with a pulse of 100, blood pressure of 170/110, and a temperature of 99.5° F. The leukocyte count was 15,000. Urinalysis revealed a specific gravity of 1.015, 3+ albuminuria, and an occasional red blood cell.

Roentgenographic Findings.

Intravenous Pyelography. The preliminary roentgenogram of the abdomen showed a moderate degree of ileus with a partially obliterated left psoas shadow and loss of the lateral contour of the left kidney. The kidneys were equal in size (Fig. 11). Excretion was prompt on the right, with a normal collecting system and ureter. On the left there was delayed excretion, with no filling of the middle calyx and infundibulum and poor filling of the upper and lower pole collecting systems (Fig. 12).

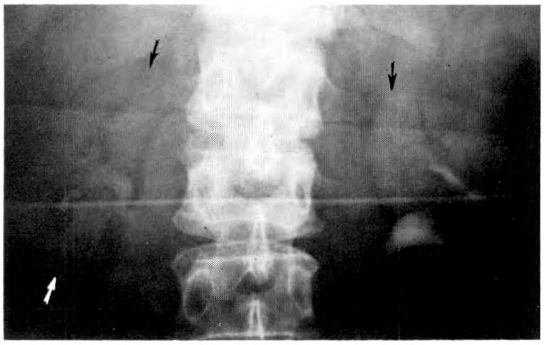

Fig. 10. Case II. Diminution in size and return of partial function on the right, 4 weeks post infarction.

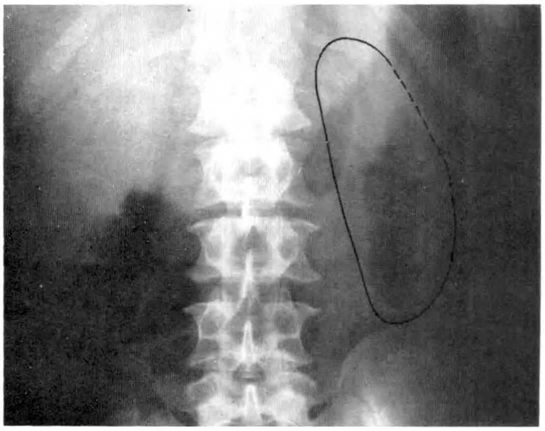

Fig. 11. Case III. Plain roentgenogram of the abdomen showing partial obliteration of left psoas shadow and loss of the lateral contour of the left kidney.

Renal Angiography. The right renal arterial supply was unremarkable. The left main renal artery was patent. The segmental artery supplying the middle portion of the left kidney was obstructed (Fig. 13). In the nephrographic phase an infarct was outlined by a wedge-shaped defect in the middle third of the left kidney. Extending from this region along the lateral margin of the kidney to the upper pole was a band-shaped nephrographic defect (Fig. 14).

Comment. Arteriography localized the site of embolization and confirmed the diagnosis.

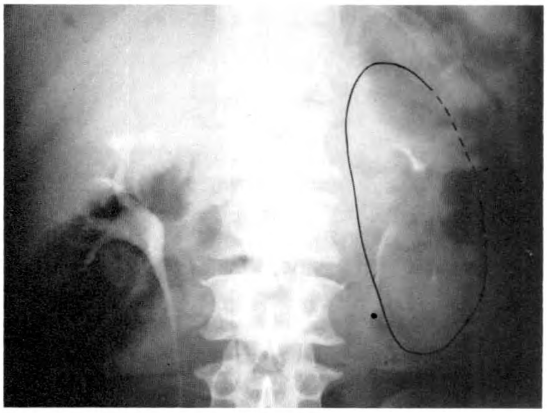

Fig. 12. Case III. Intravenous pyelogram showing lack of filling of the middle calyceal system with decreased opacification of the upper and lower pole collecting system.

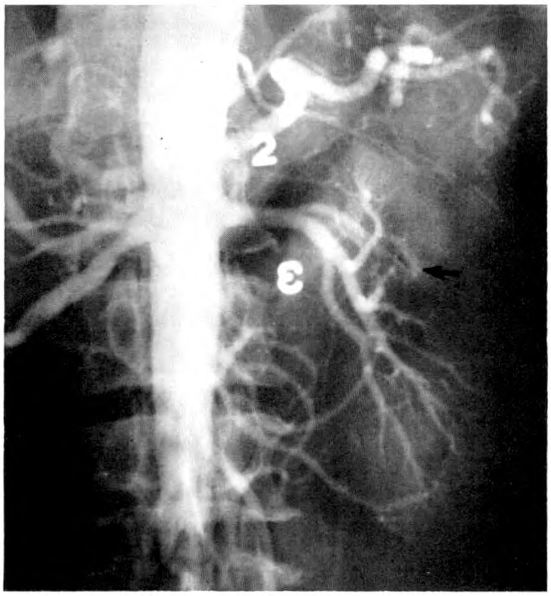

Fig. 13. Case III. Angiogram showing obstruction of a segmental artery to the middle portion of the left kidney (arrow).

Case IV. M.M., a 68 year old white female, was admitted to the hospital because of acute pulmonary edema. Diagnoses of coronary artery disease with chronic congestive heart failure, and an old myocardial infarct had been made in the past. Three days after admission, severe left costovertebral angle pain developed. No nausea, vomiting, or urinary tract symptoms were noted.

Pertinent physical findings included tenderness in the left costovertebral angle, atrial fibrillation with a rate of 130, blood pressure of 140/80, and a temperature of 100.5° F. Urinalysis revealed a specific gravity of 1.015, 3+ albuminuria, and 10 or 12 red blood cells.

Roentgenographic Findings.

Intravenous Pyelography. The plain roentgenogram disclosed a moderate degree of ileus with well delineated psoas shadows but poorly outlined kidney contours. The right kidney was ectopic, with the lower half overlying the iliac crest. The ureteropelvic junction was displaced laterally. Function on the right was normal. There was a small amount of excretion in the upper major calyx on the left. The remaining collecting structures were not outlined. The size of the left kidney could not be determined (Fig. 15).

Retrograde Pyelography. The left collecting

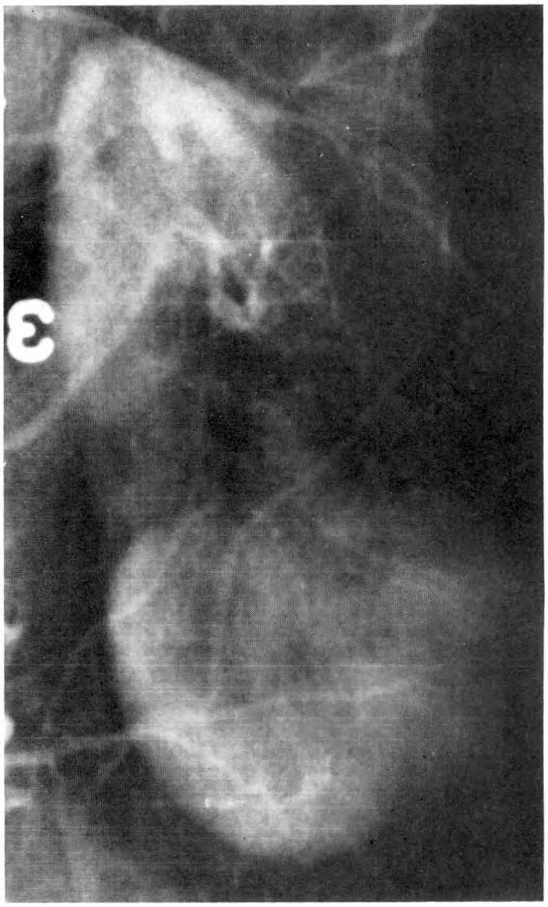

Fig. 14. Case III. Wedge-shaped defect in the mid-portion corresponding to the area of infarction.

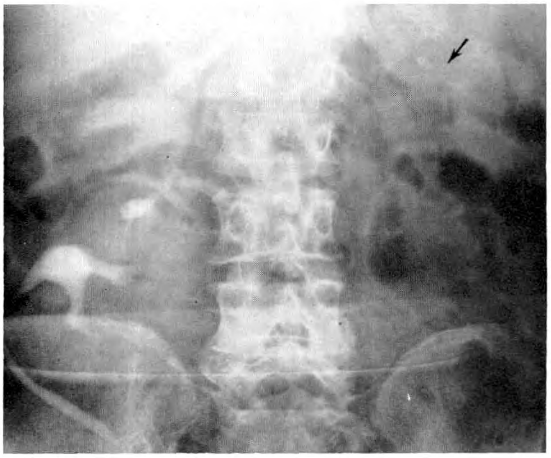

Fig. 15. Case IV. Intravenous pyelogram showing ectopy of the right kidney with only the collecting system of the upper pole on the left faintly opacified.

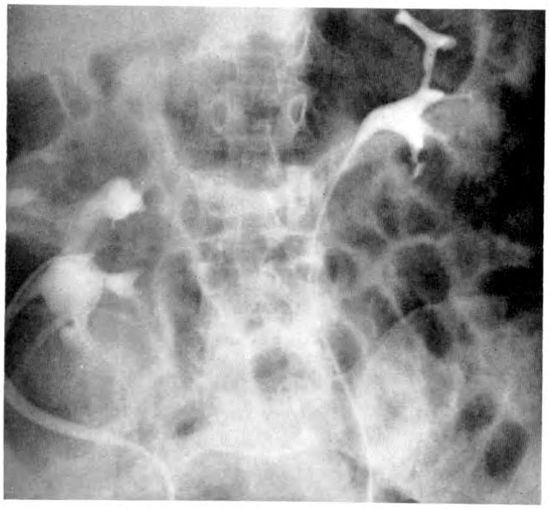

Fig. 16. Case iv. Retrograde pyelogram showing a normal left collecting system.

system and ureter were opacified and appeared normal (Fig. 16).

Renal Angiography. Aortography was performed by the Seldinger technique. Moderate arteriosclerosis of the aorta and iliac arteries was apparent. The right kidney was supplied by three branches which arose from the lower portion of the aorta, right common iliac, and left common iliac artery, respectively (Fig. 17).

On the left, the main renal artery was patent. The segmental branches supplying the middle and lower portions of the kidney were occluded. The intralobular branches in the upper pole showed some diminution (Fig. 18). There was a nephrographic phase in the upper pole of the left kidney but none in the middle and lower sections.

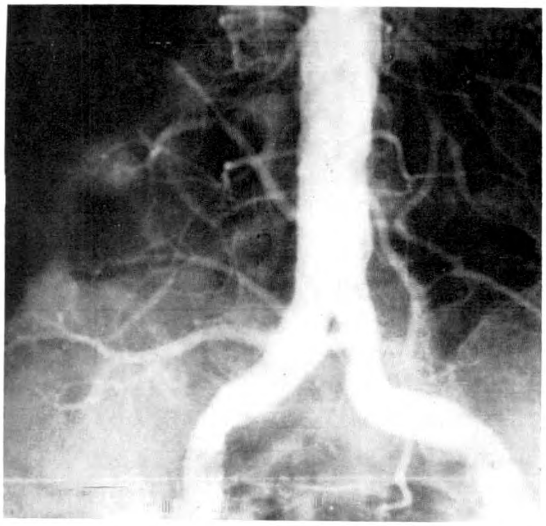

Fig. 17. Case iv. Aortogram showing anomalous blood supply to the ectopic right kidney.

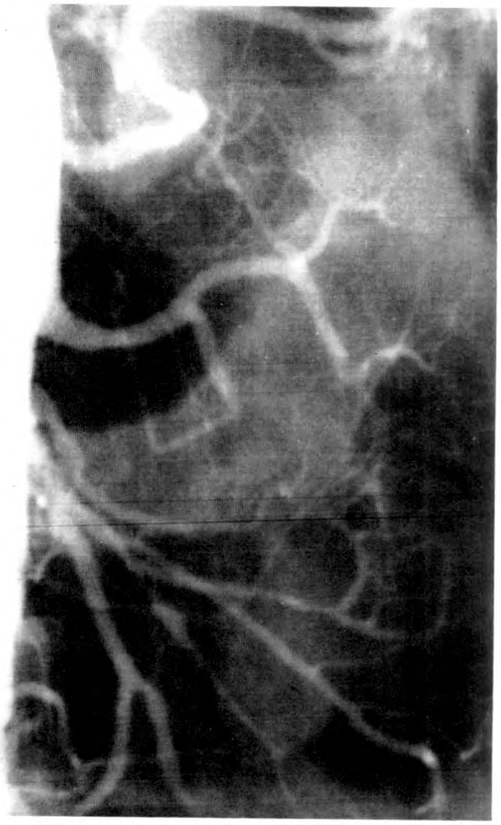

Fig. 18. Case iv. Angiogram showing occlusion of the segmental branches of the middle and lower portions of the left kidney with decrease in the intralobular arteries in the upper pole.

Subsequent Course. An intravenous pyelogram 21 days later showed no change in the appearance of the kidneys and collecting structures.

Comment. Retrograde pyelography revealed normal calyces, although function was shown to be markedly diminished on the intravenous study. Angiography confirmed the diagnosis.

Case v. J.M., a 43 year old white male,[3] was admitted to the hospital because of right flank pain of 18 hours' duration. The patient had been hospitalized 4 years previously because of an enlarged heart. Following an extensive cardiac work-up, a diagnosis of probable adult fibroelastosis was made. No urinary tract symp-

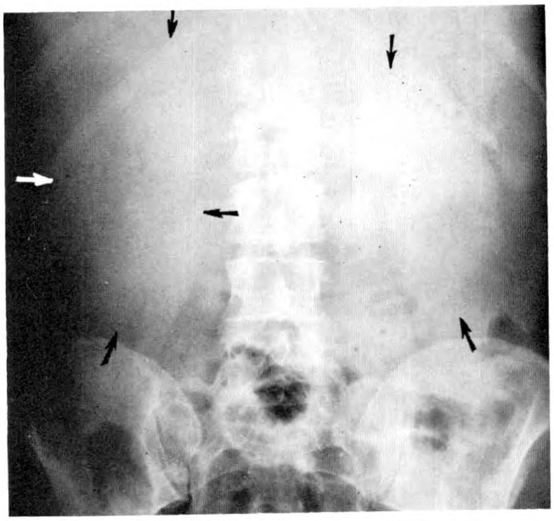

Fig. 19. Case v. Plain roentgenogram revealing slight enlargement of the right kidney with minimal loss of the right psoas shadow.

toms were evident; vomiting had occurred twice.

Pertinent physical findings included tenderness at the right costovertebral angle, cardio megaly, atrial fibrillation with a pulse of 87, blood pressure of 140/100, and a temperature of 102° F. The leukocyte count was 17,000. Urinalysis revealed a specific gravity of 1.006, 4+ albuminuria, and 4–6 red blood cells.

Roentgenographic Findings.

Intravenous Pyelography. The plain roentgenogram of the abdomen revealed a normal bowel gas pattern. There was a slight loss of the right psoas shadow. The right kidney was a little larger than the left. The measurements were 14 cm.×9 cm. on the right and 12 cm.×6.5 cm. on the left (Fig. 19). The collecting system and ureter were normal on the left. Along with enlargement of the kidney on the right, there was generalized stretching of the collecting structures. The calyces and infundibula filled incompletely in the middle section of the kidney (Fig. 20).

Subsequent Course. The right kidney was explored, and thrombosis of the main renal artery was found. An aberrant vessel to the upper pole was patent. The kidney was markedly swollen, especially the lower pole, which contained multiple yellow areas of infarction; only a few such areas were seen in the upper pole. There were also patches of incomplete infarction with necrotic tubules but viable glomeruli. The infarct was thought to be of about 1 week's duration. A right-sided nephrectomy was performed.

Two weeks following discharge, the patient re-entered the hospital and died of multiple pulmonary emboli. At autopsy, mural thrombosis was found in both ventricles and atria. The final diagnosis was idiopathic fibroelastosis.

Comment. The affected kidney in this case was larger than the normal kidney.

ROENTGEN OBSERVATIONS

Although the clinical findings may suggest renal infarction, the diagnosis is usually made radiographically. Evaluation may include roentgenography of the abdomen, intravenous pyelography, retrograde pyelography, and renal angiography. The changes seen on the abdominal roentgenogram are usually nonspecific, but may suggest the diagnosis. Varying degrees of ileus, obliteration of the psoas shadows, and/or of the kidney outline, may be observed. Following acute infarction secondary to main artery occlusion, the renal size is usually normal, and *not* decreased. In one of our cases (Case v) the affected kidney was enlarged because of severe edema from occlusion of the main renal artery and patency of an aberrant renal vessel. Weeks after infarction, the involved kidney may reveal a considerable decrease in size. Localized indentations or atrophy of a pole may be seen following segmental infarction; calcification can sometimes occur in these scarred areas.

If infarction is clinically considered, in-

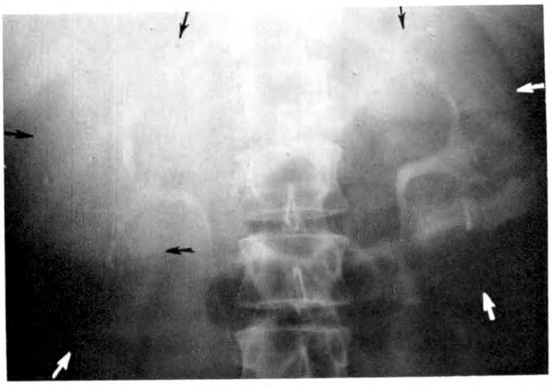

Fig. 20. Case v. Intravenous pyelogram showing stretching of the collecting system secondary to edema of the right kidney.

travenous pyelography is mandatory. No special technique is required. Frequently, there will be no function of the involved kidney or a portion thereof after the acute insult. Nonfunction is not necessarily secondary to occlusion of the main renal artery; a segmental arterial occlusion can sometimes lead to complete shutdown of renal function. If kidney function is preserved, a variety of patterns may be seen, ranging from faint opacification of a single calyx to moderately good opacification of the entire collecting system. On occasion, spreading, stretching, and incomplete filling of the collecting structures can be seen in those kidneys where severe edema follows infarction (Case v). Follow-up intravenous pyelography in the immediate postinfarction period is of limited value, since there is usually no detectable change; however, a repeat study a month or more later will usually reveal change in size or configuration of the affected kidney.

Retrograde pyelograms following the acute episode will frequently outline a normal collecting system. Nonfunction of a kidney on intravenous pyelograms coupled with a normal appearing collecting system on retrograde pyelograms is highly suspicious of arterial occlusion with or without renal infarction.

In difficult diagnostic problems, roentgenograms previously obtained are of value. An abrupt change in size or function of the kidneys should certainly suggest the possibility of acute renal infarction.

Renal angiography is indicated for those cases in which surgical intervention is contemplated.[4] This is an extremely important preoperative diagnostic study. Again, a variety of changes, ranging from complete occlusion of the main renal artery to occlusion of a single segmental branch, may be found. Obviously, surgery might be indicated only in main renal artery occlusion. In addition to localization of the exact site of arterial obstruction, a decrease in circulation time through the affected kidney may be conspicuous (Case ii). Furthermore, study of roentgenograms obtained in the nephrographic phase are helpful in evaluating the total blood supply and will outline infarcted areas in more detail (Case ii). If kidney function is considerably impaired due to multiple emboli in the smaller branches of the kidney, a decrease or absence of the nephrographic density is apparent. Sequential roentgenograms are invaluable.

SUMMARY

Twelve cases of acute arterial renal infarction with their clinical background and roentgenographic findings are reviewed. Five representative examples are presented in detail.

Sudden onset of nonspecific abdominal pain is the predominant symptom. Microscopic hematuria and albuminuria are frequent urinary findings. A definitive diagnosis can be established only by roentgenographic means. The intravenous pyleogram is an important diagnostic study and shows nonfilling of calyceal structures, with distortion and stretching, or nonfunction of an entire kidney. A retrograde pyelogram demonstrates normal architecture of the collecting system.

The renal angiogram will localize the lesion and delineate the extent of the infarct.

In some cases emergency surgery will save the involved kidney.

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RENAL ARTERY SPASM SIMULATING ORGANIC DISEASE*

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SPASM of arteries in response to external stimuli has been recognized roentgenographically since intra-arterial injections of opaque material were first made. Spasm of the intracranial arteries, particularly when associated with intracranial hemorrhage,[11] and spasm of the brachial artery[2] are familiar examples. The contraction usually is brief, and normal circulation is restored without evidence of tissue damage. However, when severe and prolonged spasm involves the blood supply to a sensitive organ, permanent injury may result.[6,14]

Because arterial spasm may simulate an organic lesion, its recognition is important to avoid an erroneous diagnosis. The purpose of the authors is to report 3 cases of renal artery spasm shown by selective arteriography and to discuss arterial spasm in general.

REPORT OF CASES

CASE I. A 34 year old Negro male was admitted to the hospital because of left flank pain. An intravenous urogram showed slight displacement of the lower calyces of the left kidney. Selective left renal arteriography was performed to exclude renal cell carcinoma. A stenotic area was demonstrated immediately proximal to the bifurcation of the renal artery (Fig. 1*A*). Repeat study following withdrawal of the tip of the catheter to the orifice of the renal artery showed a normal vessel (Fig. 1*B*). At exploration of the kidney 1 day later, a large, organized perinephric hematoma was found. The kidney was palpated and appeared grossly normal.

CASE II. A 28 year old Negro male was admitted to the hospital because of microscopic hematuria. Intravenous urography was normal. Selective right renal arteriography was performed with the catheter positioned at the orifice of the vessel. The ventral branch of the renal artery immediately distal to the bifurcation appeared corrugated (Fig. 2*A*), somewhat resembling fibromuscular hyperplasia. Re-examination 15 minutes later no longer showed these irregularities (Fig. 2*B*).

CASE III. A 39 year old Negro female was admitted to the hospital because of chronic renal disease. Selective renal arteriography was performed immediately before and after renal biopsy to evaluate possible vascular changes resulting from the procedure. The catheter remained in place during the biopsy and was flushed with continuous saline-heparin drip. The pre-biopsy study demonstrated normal renal arteries (Fig. 3*A*). The examination performed 15 minutes after biopsy showed absent filling of the branch of the dorsal artery supplying the lower pole (Fig. 3*B*). An intravenous urogram the next day showed no change when compared with a pre-biopsy examination.

DISCUSSION

SPASM DURING ARTERIOGRAPHY

Spasm during arteriography may be the result of one or more of the following stimuli: (1) mechanical irritation caused by needles, catheters, guide wires,[12] or jet of injected material, or (2) chemical or osmotic irritation due to contrast material, vasoconstricting agents, or extravasated blood.[5,6,8]

Lende[11] and Kinmonth[9] have shown that arteries can respond to irritants by a sustained contraction of smooth muscle. The spasm is a local response which is independent of autonomous nervous fibers, since it occurs even in the absence of the adventitia. Furthermore, electric stimulation of the nerve fibers fails to affect the arteries. Mustard and Simmons[13] have produced spasm merely by stretching the arteries in dogs. Abrams *et al.*[1] and De Maria *et al.*[5] produced renal artery spasm immediately

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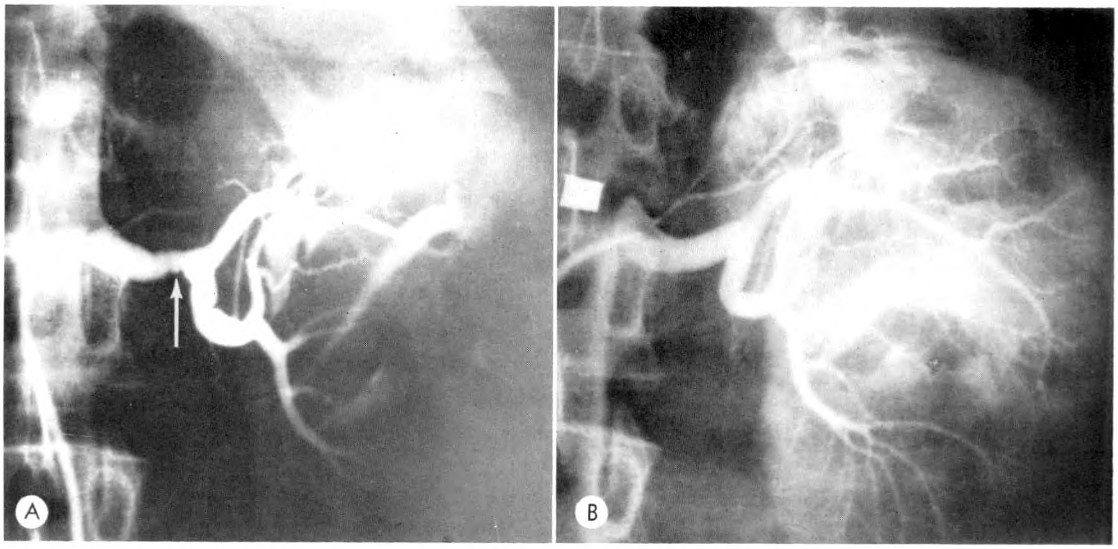

Fig. 1. Case I. *Selective left renal arteriograms.* (*A*) Spasm of the left renal artery is shown immediately proximal to its bifurcation (↑) ½ second after the beginning of injection. The catheter has recoiled into the aorta. (*B*) A second injection approximately 15 minutes later shows a normal renal artery.

proximal or distal to the first bifurcation by intravenous injections of epinephrine.

Arterial spasm may produce partial or complete occlusion of the vessel, and it may last from a few seconds to many hours. Sensitive organs may be irreparably damaged when spasm is prolonged.[6,14] Trauma may produce such severe arterial spasm that little or no bleeding occurs immediately following injury or even amputation of an extremity.[3,10,12]

Frequency of spasm is inversely propor-

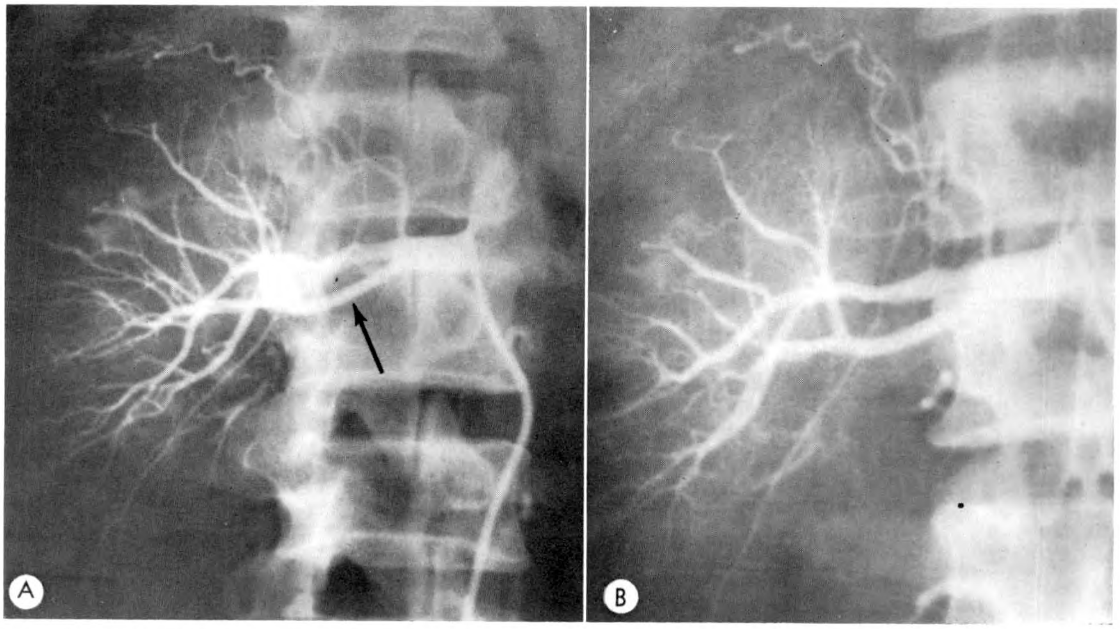

Fig. 2. Case II. *Selective right renal arteriograms.* (*A*) Concentric irregularities (↖) are shown in the ventral branch distal to the first bifurcation. (*B*) A second injection 10 minutes later shows a normal ventral branch.

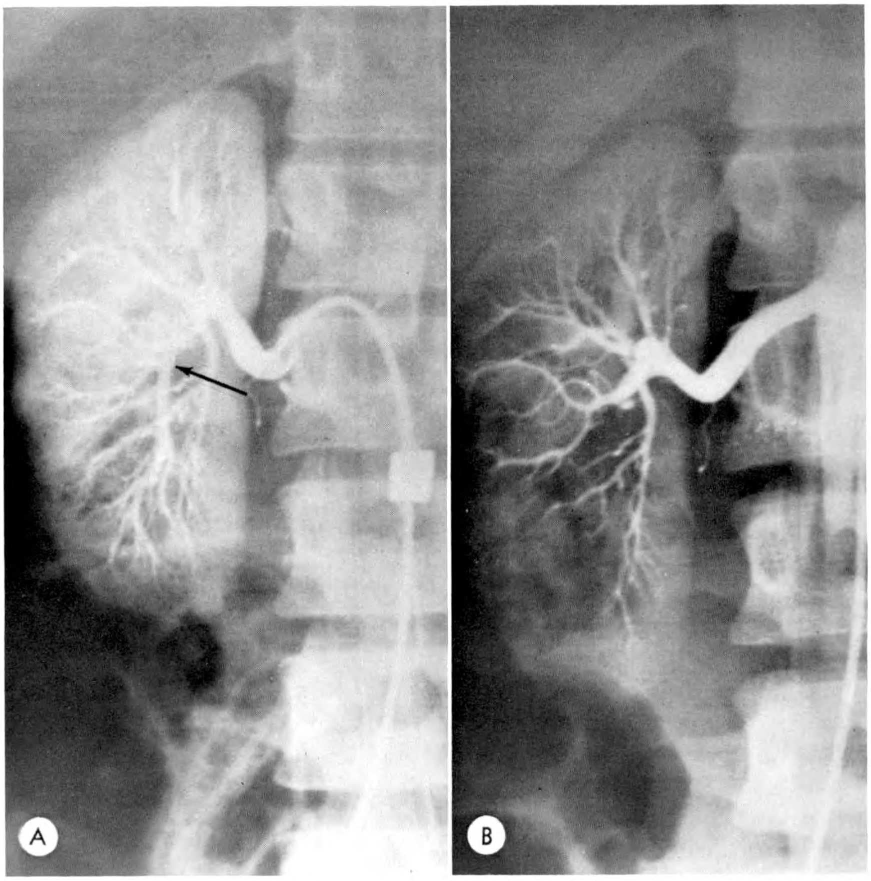

FIG. 3. Case III. *Selective right renal arteriograms.* (*A*) The renal arteries are normal. (*B*) Repeat arteriogram 15 minutes after renal biopsy shows absent filling of the branch of the dorsal artery supplying the lower pole. Other investigators[4,6,7] have documented cases of spasm causing completely absent opacification of a segmental renal artery.

tional to the size of the vessel. Medium-sized, muscular type arteries usually are involved. The deep femoral, popliteal, brachial and internal carotid arteries contract easily, whereas the femoral, axillary, common carotid and proximal main renal arteries rarely are affected. Involvement of elastic type vessels is even more unusual, and complete occlusion of this type of vessel due to spasm cannot be produced.[12]

Wickbom and Bartley[14] as well as Lindbom,[12] have pointed out that approximately 75 per cent of patients in whom peripheral arterial spasm occurs are younger than 30 years and only 5 per cent are over the age of 60. They offer the explanation that with advancing age fibrosis replaces the muscular fibers in the media of the arteries, limiting their ability to react to irritating stimuli. Spasm is more frequent in women than men, and a very high incidence is encountered in patients with clinical signs of Raynaud's disease. Preexisting damage or disease of the arterial wall may be a predisposing factor.[6]

Roentgenographically, spasm may be difficult to distinguish from organic stenosis due to arteriosclerosis, fibromuscular hyperplasia, or Buerger's disease. Spasm of a large artery may simulate the corrugations of a dacron graft.[7]

RENAL ARTERY SPASM

Four cases of renal artery spasm previously have been reported. The first case was described in 1959 by Boijsen[4] in his monograph on renal arteriography. In 1963, 2 additional cases were reported by Haage and Rahm.[6] The spasm was demonstrated during selective renal arteriography, but was not present when the contrast material was injected into the aorta. In the first case of Haage and Rahm, the spasm developed in the main renal artery distal to an area of slight stenosis. In their second case, several injections were made. The degree of spasm progressed with each injection, until finally the branch of the dorsal artery supplying the lower pole no longer was opacified. Two days later a nephrectomy was performed, and a fresh infarct was found corresponding to the area supplied by the contracted branch. The arteries were examined carefully, but no organic lesion was present. The authors concluded that spasm caused the progressive nonopacification of the vessel and produced the renal infarct. Recently, in a paper describing angiographic artefacts Herbert[7] cited a case in which sudden peripheral spasm occurred during selective renal arteriography. The spasm could have been mistaken for organic occlusion had serial roentgenograms not been obtained.

In our cases during selective renal arteriography, transient narrowing and irregularity involved the main renal artery in 1 patient (Case I) and the renal artery branches in another (Case II). In both patients the appearance of the arteries promptly returned to normal following withdrawal of the catheter. In Case III we can only speculate that nonopacification of the vessel was due to spasm, possibly related to the renal biopsy. During biopsy, some bleeding into the surrounding tissue always occurs, and the contraction may have been caused by a mechanism similar to that occurring in intracranial hemorrhage. If the artery itself had been injured by the biopsy needle, extravasation of the contrast material probably would have occurred. The roentgenographic findings in this case are very similar to those reported by Boijsen,[4] Haage and Rahm[6] and Herbert.[7] The normal intravenous urogram obtained the following day further supports the likelihood that spasm was the cause of nonopacification of the vessel.

All cases of renal artery spasm have occurred during selective renal artery catheterization. In the 1 reported case in which a tertiary branch was involved, prolonged contraction resulted in an infarct.[6] During selective renal arteriography, catheters should be left in place as briefly as possible. Spasm should be recognized promptly and the catheter withdrawn immediately, although injection of a vasodilator drug into the artery first may be advisable. When the diagnosis is uncertain, a repeat examination with a mid-aortic injection may be required to determine the consistency of the findings.

SUMMARY

Three cases are reported of renal artery spasm demonstrated during selective renal arteriography. The arteriographic appearance of renal artery spasm has no characteristic features and may simulate organic stenosis. Spasm must be recognized to avoid an erroneous diagnosis.

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ANGIOGRAPHIC STUDY OF THE EFFECT OF VASOPRESSORS ON RENAL VASCULARITY (METARAMINOL)*

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IN A previous study,[1] renal angiography was used to investigate the effects of epinephrine and levarterenol on the kidney vascularity. Both drugs produced similar effects, although levarterenol appeared more potent than epinephrine. In small doses, vasoconstriction takes place at the peripheral vessels with diminution in the vascular nephrogram, dilatation of the main renal artery and of the interlobar arteries, and prolongation of the arterial phase with late filling of the veins. Large doses produce marked and sudden constriction of the main renal artery close to its site of major branching with little filling of the interlobar vessels which appear attenuated, as well as marked diminution in the intensity of the nephrogram with very late, if any, opacification of the veins. There was no evidence of a "Trueta" shunt[3] at any of the tested doses of these two vasopressors. It was also demonstrated that both epinephrine and levarterenol have a direct action on the renal vessels.

The present report deals with the effects of another vasopressor on renal vascularity—metaraminol.

METARAMINOL

Weil[5] reported that metaraminol (aramine) produces only a slight decrease of renal blood flow in normotensive dogs as compared to more marked decreases with norepinephrine. Patients in profound shock were treated with metaraminol in single intravenous doses of 3 to 15 mg. with the blood pressure rise reaching a peak in 5 minutes and continuing for 25 minutes.

Spoerel *et al.*[2] reported deterioration in patients treated by continuous intravenous infusion of metaraminol. There was intense vasoconstriction and stagnation of the peripheral circulation. They stated that the kidney especially shows prolonged vasoconstriction with metaraminol.

Udhoji and Weil[4] discussed the questionable value of vasopressor agents in the treatment of shock, where the arterial vascular bed is already constricted. This, of course, also holds true for the kidney; in shock there is already reduced renal blood flow and lowered urine flow. On the basis of their studies on 12 patients with hypotension and clinical features of shock, they established a dose ratio of metaraminol to levarterenol; it takes 5 times the dose of metaraminol than that of levarterenol to produce similar clinical response.

TECHNIQUE

As described previously,[1] renal angiographies were done on the dog. Most of our studies consisted of selective catheterization of the renal artery with the Seldinger technique, using thorotrast as the contrast medium. Reproducibility of the injection factors was assured in respect to pressure of injection (speed of delivery of the bolus of the opaque medium), amount of contrast material delivered and initiation of the roentgen-ray exposures at the same time in the course of the injection. Usually, roentgenograms were taken at the speed of 2 per second for a total of 5 seconds. Intra-aortic blood pressure was continuously monitored during an experiment. Single dose intravenous administration of the tested drug was used for the most part. Angiograms were made at the height of the blood pressure response, $2\frac{1}{2}$ minutes after

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completion of the intravenous injection of the metaraminol.

RESULTS

In intravenous dose of 0.05 and 0.1 mg. per kg., metaraminol effected dilatation of the main renal artery and its major branches, dilatation of the interlobar arteries, maintenance of the normal vascular nephrogram, and normal appearance of the intrarenal and main renal veins. The arteries emptied of the opacified blood at the same time interval as in the control angiograms; the veins filled and emptied as in the control with slight dilatation of intrarenal veins in some experiments (Fig. 1, *A–F*). According to the estimates of Udhoji and Weil,[4] 0.05 to 0.1 mg. metaraminol corresponds to 10 to 20 μg. of levarterenol. As reported previously,[1] 10 to 20 μg. of levarterenol produce profound effects on the renal vascularity, consisting of constriction of the major renal artery branches, diminution in size of the interlobar arteries, decrease in the intensity of the nephrogram, and late and poor filling of the veins—indicating increased resistance at the level of the major renal arteries. Even smaller doses of levarterenol (0.5 to 1.0 μg. per kg.) had shown evidence of increased vascular resistance, manifested by slowing of the vascular phases and diminution in the intensity of the nephrogram. As far as could be judged from the angiogram, metaraminol in dosage of 0.05 to 0.1 mg. per kg. caused no decrease in renal blood flow. In fact, there is the suggestion of increased renal blood flow. A dose of 0.1 mg. of metaraminol per kg. resulted in an average increase in the mean systemic blood pressure of 80 mm. Hg. With levarterenol in dose of 15 μg. per kg., the mean blood pressure rose 90 mm. Hg.

At higher doses of metaraminol, such as 0.2 to 0.4 mg. per kg., the changes were like those produced by high doses of epinephrine or levarterenol, consisting of sudden and marked constriction of the main renal artery at or near its bifurcation, dilatation of the renal artery proximally, attenuation of the interlobar arteries, decrease in intensity of the nephrogram, poor opacification

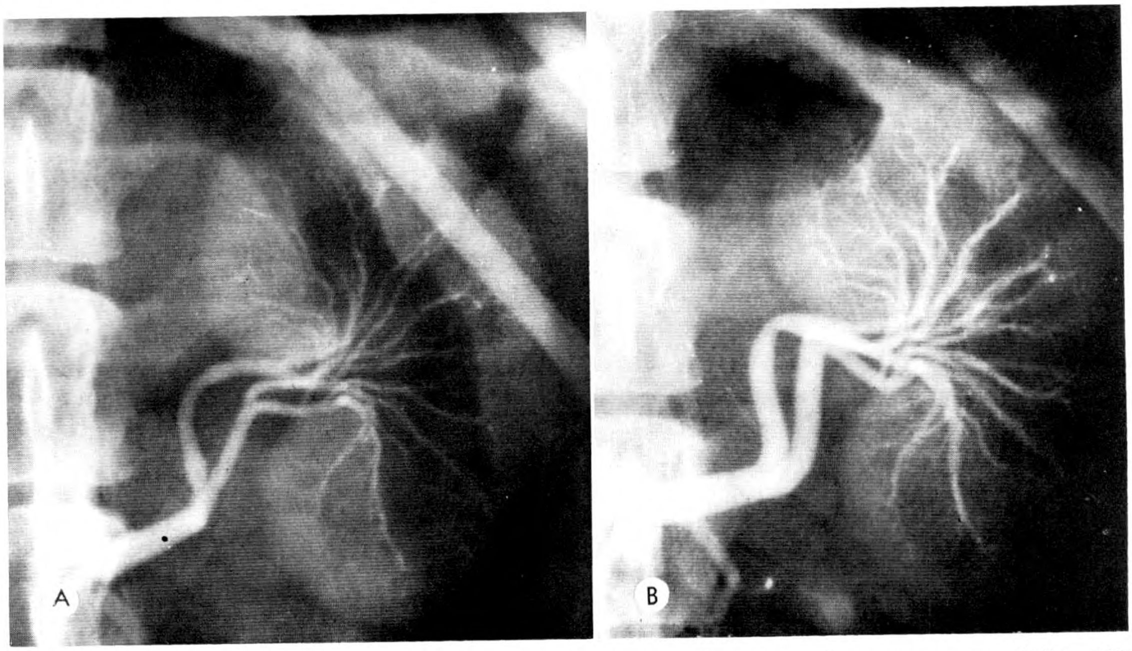

Fig. 1. (*A*) Control thorotrast angiogram, 1 second after the injection of the thorotrast, 1 second film. (*B*) Thorotrast angiogram, 1 second film, after intravenous administration of metaraminol, 0.1 mg. per kg., shows dilatation of the main renal artery as well as of the segmental and interlobar arteries.

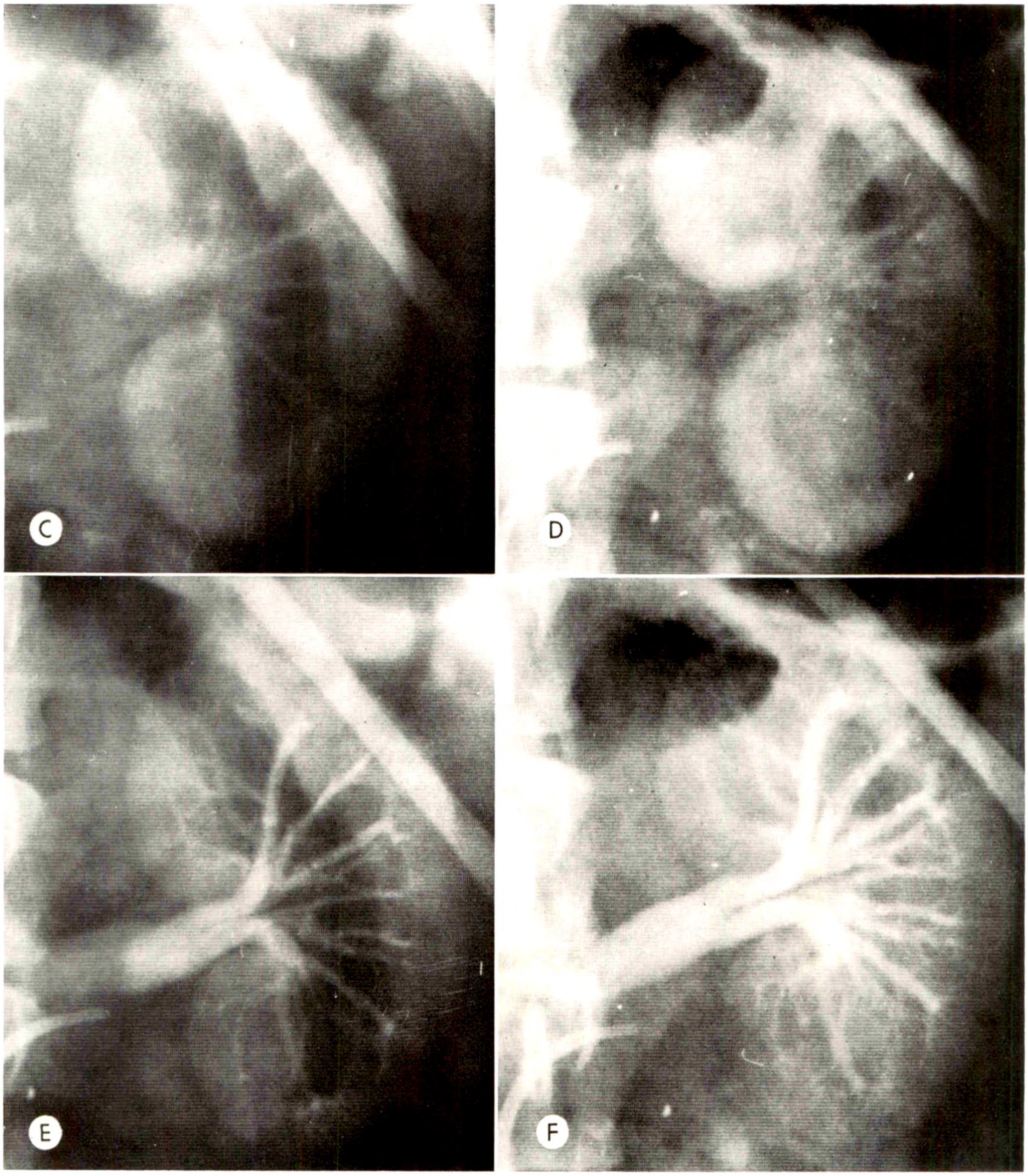

Fig. 1. (*C*) Control angiogram, 1.5 second film, shows a good vascular nephrogram. (*D*) Post-metaraminol angiogram, 1.5 second film, shows a good vascular nephrogram, equal in intensity to that of the control (*C*). (*E*) Control angiogram, 2.5 second film, shows good venous opacification. (*F*) Post-metaraminol angiogram, 2.5 second film, shows venous opacification, the veins being wider than in the control (*E*).

of the intrarenal and main renal veins, evidence of slowed circulation (prolongation of the vascular phases) and, usually, decrease in size of the kidney (Fig. 2, *A–F*). The extent of angiographic changes was related to the dose of the metaraminol (Fig. 3). It is of interest that in several experiments with a high dose of metaraminol the ureteral artery was well opacified in spite of its origin from a narrowed segmental artery beyond the constriction of the renal artery. In such cases the ureteral artery was better visualized than in the control angiogram, where, in fact, it may not be opacified at all. As with epinephrine and levarterenol, so too with metaraminol, high doses increase renal vascular resistance with a major effect on the main renal arteries.

MECHANISM OF ACTION

As reported previously,[1] angiographic studies indicated that epinephrine and levarterenol have a direct action on the renal vessels and do not produce their effects wholly by way of increased blood pressure. Similar studies were done with metaraminol. A catheter was inserted percutaneously into each femoral artery and passed in retrograde manner to the renal arteries, accomplishing catheterization of each renal artery. Control angiography was performed with thorotrast (0.4 cc. per kg.), the contrast medium being injected by the automatic injector (Cordis) simultaneously into both catheters through a Y-connector. Then metaraminol (0.2 mg. per kg.) was injected via the catheter into the right renal artery, followed immediately by a repeat angiogram under the same conditions as for the control angiogram. The angiography was completed before the occurrence of any change in systemic blood pressure. On the right side, there was marked constriction just beyond the bifurcation of the main renal artery, the renal artery remaining opacified during the 5 seconds of the study with no advance of the opaque material into the interlobar arteries. On the left side, the angiogram appeared the same as the control (Fig. 4, *A–D*). These results indicate that metaraminol also has a direct action on the renal vessels.

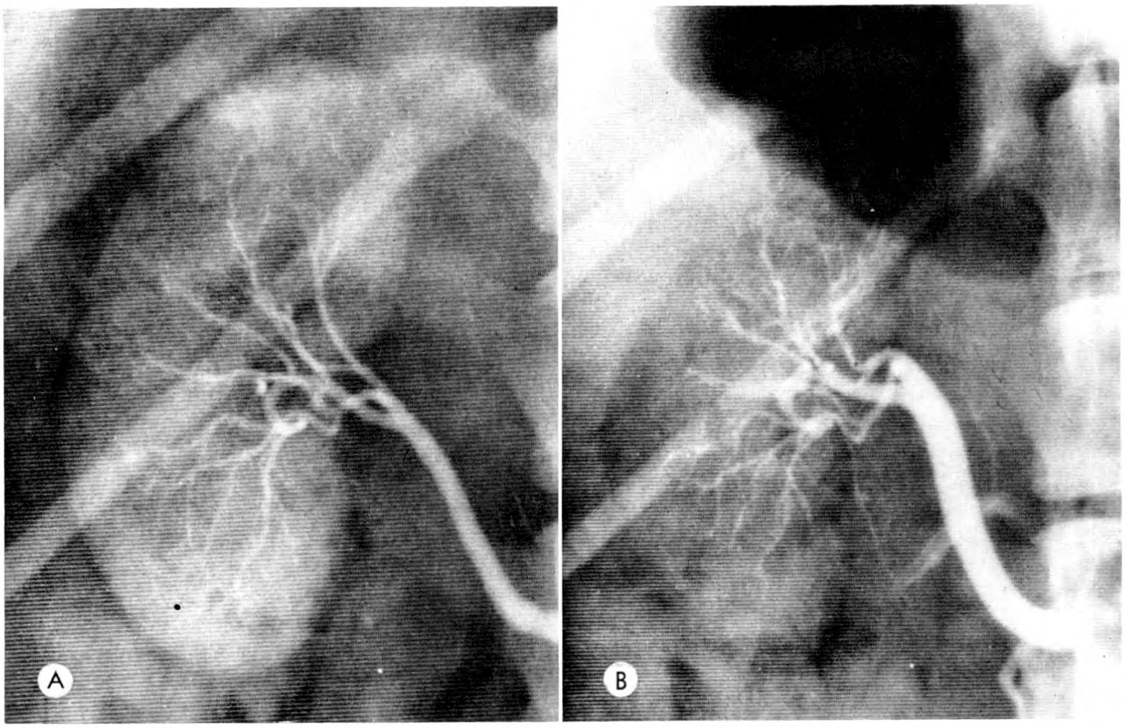

Fig. 2. (*A*) Control thorotrast angiogram, 1 second film. (*B*) Thorotrast angiogram, 1 second film, after intravenous administration of metaraminol, 0.2 mg. per kg., shows dilatation of the main renal artery with narrowing beyond its bifurcation and attenuation of the interlobar arteries which appear tortuous.

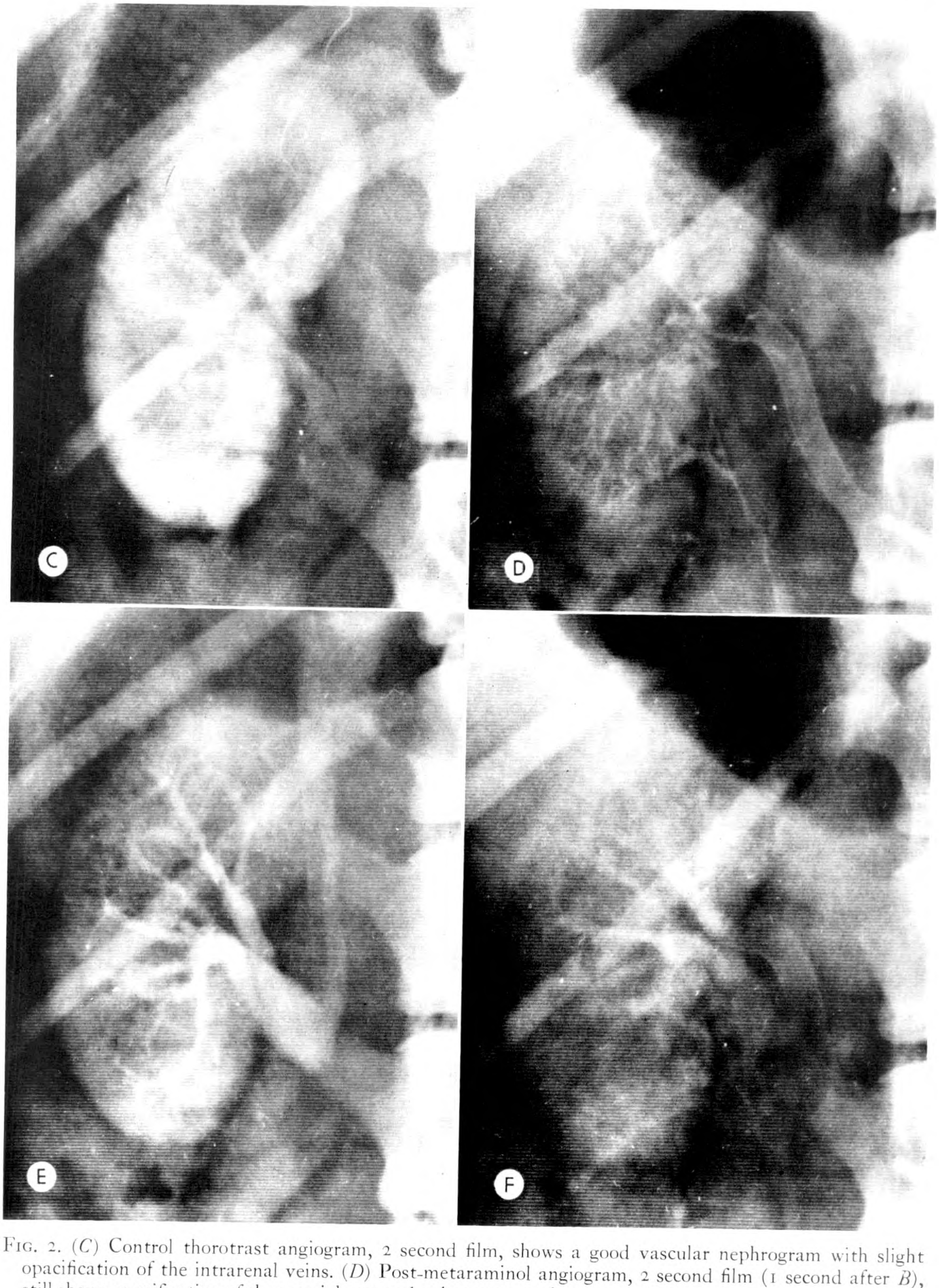

FIG. 2. (*C*) Control thorotrast angiogram, 2 second film, shows a good vascular nephrogram with slight opacification of the intrarenal veins. (*D*) Post-metaraminol angiogram, 2 second film (1 second after *B*), still shows opacification of the arterial tree and only a poor nephrogram. (*E*) Control thorotrast angiogram, 3 second film, shows good opacification of the intrarenal veins, main renal vein and inferior vena cava. (*F*) Post-metaraminol angiogram, 3 second film (1 second after *D*), shows poor venous opacification.

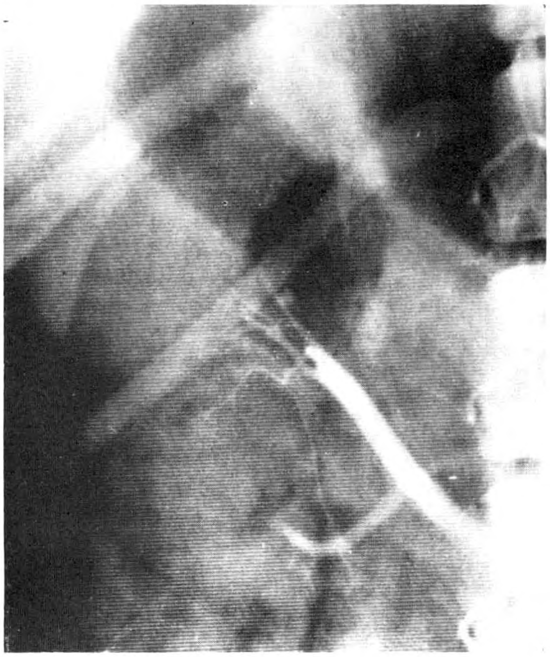

FIG. 3. Same dog as in Figure 2, *A–F*. Thorotrast angiogram after metaraminol, 0.4 mg. per kg., 3.5 second film, shows more pronounced arterial changes than seen with 0.2 mg. per kg. Note good opacification of the ureteral artery.

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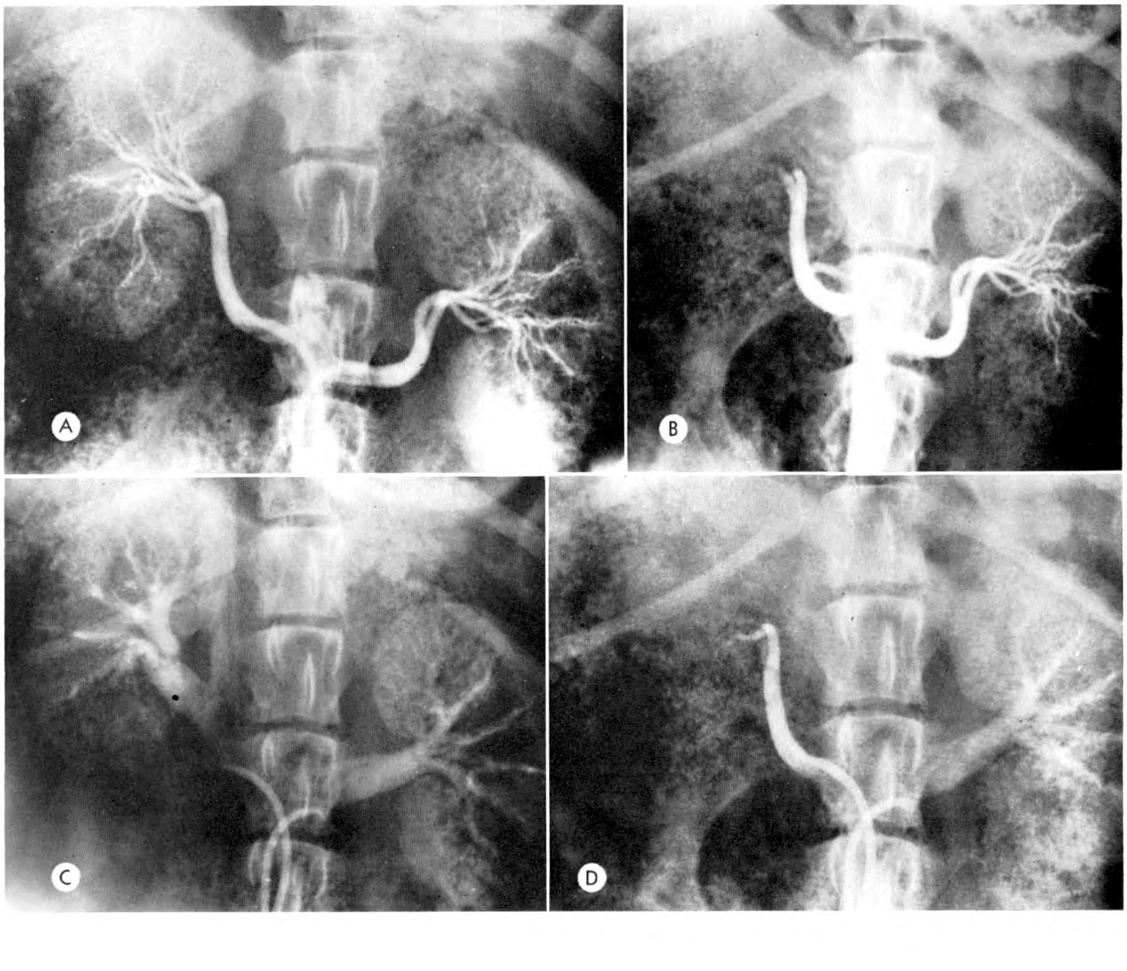
SUMMARY

Angiographic study has been made of the effects of metaraminol on the renal vessels of the dog.

As far as could be judged from the angiogram, metaraminol in dosage of 0.05 to 0.1 mg. per kg. caused no decrease in renal blood flow.

With higher dose (0.2 to 0.4 mg. per kg.)



metaraminol produced marked changes in the appearance of the renal vessels, indicating increased renal vascular resistance with a major effect on the main renal arteries.

Doses of metaraminol and levarterenol with similar effects on the blood pressure showed different activities in respect to renal vasoconstriction. Levarterenol (like epinephrine) is more potent than metaraminol in respect to constriction of renal vessels.

Metaraminol has a direct action on the renal vasculature.

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Fig. 4. (*A*) Control simultaneous bilateral selective angiogram, 1 second film, shows normal appearing renal arteries bilaterally. (*B*) Bilateral angiogram immediately after administration of metaraminol, 0.2 mg. per kg., into the right renal artery, 1 second film, shows marked constriction just beyond the bifurcation on the right side. The renal arterial tree on the left is unchanged from its control appearance (*A*). (*C*) Control bilateral angiogram, 2.5 second film, shows good opacification of the renal veins bilaterally. (*D*) After metaraminol into the right renal artery the angiogram, 2.5 second film, still shows the marked constriction of the right renal artery with no progress of the thorotrast into segmental arteries, the appearance remaining unchanged from that of the 1 second film (*B*). On the left side there is good venous filling, as in the control (*C*).

NEPHROTIC SYNDROME SECONDARY TO RENAL VEIN THROMBOSIS*

THE VALUE OF INFERIOR VENA CAVOGRAPHY

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THE nephrotic syndrome is that clinical entity consisting of albuminuria, hypoalbuminemia, and edema. The etiology is unknown; over a dozen different conditions can act as predisposing factors, including such systemic diseases as lupus erythematosus and amyloidosis, exposure to drugs or heavy metals, circulatory disturbances such as renal vein thrombosis and constrictive pericarditis, and to these may be added the idiopathic forms secondary to intrinsic renal disease.[7]

The radiologist plays a key role in diagnosing those cases secondary to renal vein thrombosis; it is the purpose of the author to report one such case, and specifically to emphasize the value of vena cavography in establishing the exact diagnosis. Three methods of opacifying the inferior vena cava will be discussed; *i.e.*, by direct vena cava injection, either from below or above, and by the intra-osseous route.

We are not concerned with renal vein thrombosis secondary to malignant tumor (the most common etiology) or with renal phlebitis secondary to ascending infection, as commonly seen in children. In adults the nephrotic syndrome secondary to venous thrombosis is the result of spontaneous caval thrombosis. The pathophysiology is poorly understood, but it is postulated that the peritubular capillaries receive the burden of the increased venous back pressure, and that this causes tubular and/or glomerular damage. This damage permits the leakage of albumin into the urine with consequent lowering of the level of plasma albumin.[1]

The changes on the pyelogram, whether intravenous or retrograde, have been well documented by Zheutlin *et al.*[11] During intravenous pyelography the concentration of contrast material can vary from none to normal. The kidneys are usually large and may appear polycystic. Retrograde findings vary from simple irregularity and incomplete filling of the renal pelvis to frank diffusion of the contrast agent into the renal parenchyma. This range of findings is quite compatible with the possible stages of venous thrombosis. For example, an acute thrombosis might well lead to a nonfunctioning large kidney, while a chronic thrombosis which permitted the development of collateral circulation might result in a normal appearing kidney.

Although the pyelographic picture may be suggestive of the correct diagnosis, a positive premortem diagnosis can be made only by inferior vena cavography. Harrison *et al.*[3] reported 11 cases of nephrotic syndrome secondary to renal vein thrombosis, in 4 of which a diagnosis was made roentgenologically by inferior vena cavography, and, in spite of the rapid advances made in the field of angiography since 1956, little can be added to their account. Baird and Buchanan[1] reported one case of nephrotic syndrome in which inferior vena cavography by way of a femoral venous injection demonstrated a thrombus in the inferior vena cava and renal veins. Morris *et al.*[6] also reported a case in which the diagnosis was established by percutaneous femoral vein injection. They also performed a follow-up study with a cardiac catheter inserted from the basilic vein through the superior vena cava and heart into the inferior vena cava.

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REPORT OF A CASE

A 37 year old white woman was first admitted to the Massachusetts General Hospital in October, 1963, with progressive swelling of the ankles, legs, and thighs of one month's duration. She had been placed on diuretic therapy by her local physician without results. Her weight had risen from 130 to 150 pounds over the 4 week period preceding admission. She had no other complaints and her past history was noncontributory.

On examination the blood pressure was 120/75; pulse 95 and regular; respirations 14; and temperature 98.6° F. Positive physical findings included slight peri-orbital edema, 4+ pitting edema up to the knees, and 1+ pitting edema up to the groins. Pertinent urinary findings included: specific gravity 1.029; protein 4+; occasional white blood cells, red blood cells, and hyaline casts. The hematocrit was 43 per cent; white blood cell count 7,500 with a normal differential; serum cholesterol 564 mg. per cent; serum albumin 1.5 gm. per cent and serum globulin 2.2 gm. per cent; blood urea nitrogen 8 mg. per cent; serum creatinine 0.7 mg. per cent; creatinine clearance 193.8 liters/24 hours. Urinary protein analysis done on two occasions showed losses of 5.9 gm. and 8.1 gm. per 24 hours, respectively. An intravenous pyelogram (Fig. 1) and chest roentgenogram were within normal limits. A renal biopsy was performed and, although tissue insufficient for diagnosis was obtained, there was a suggestion of thickening of the glomerular basement membrane. A diagnosis of nephrotic syndrome secondary to membranous glomerulonephritis was made, and the patient was discharged on a high-protein diet and 60 mg. of prednisone per day.

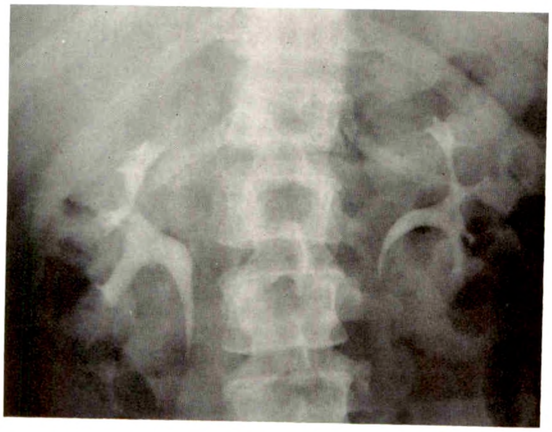

Fig. 1. Normal intravenous pyelogram.

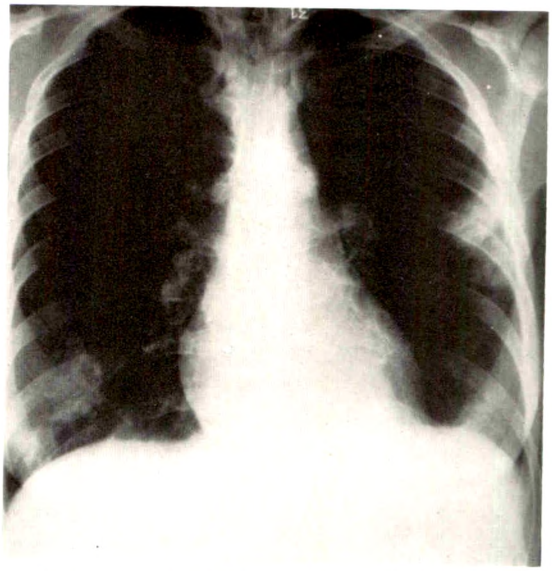

Fig. 2. Areas of infiltration and cavitation in the left mid, and right lower lung fields.

The patient did not do well and was re-admitted to the hospital in January, 1964. She had gained an additional 20 pounds in the interim. Initial laboratory values were similar to those found on her previous admission. She now had 4+ edema to the knees, 2+ edema to the inguinal ligaments, and a trace of edema over the sacrum. Three days after admission a left calf thrombophlebitis developed, followed by hemoptysis and chest pain. Chest roentgenograms were interpreted as revealing multiple cavitating pulmonary emboli (Fig. 2), and the patient was placed on anticoagulants and antibiotics. Because of contemplated venous ligation, inferior vena cavography was requested. The severe edema made direct percutaneous femoral vein puncture technically unsatisfactory and accordingly bilateral femoral intertrochanteric injections were performed. Only the right distal iliac vein could be opacified, while a large number of abnormal collateral channels were seen bilaterally (Fig. 3 and 4). It was felt that this appearance was secondary to increased inferior caval back pressure. A catheter was then inserted into the right basilic vein, threaded in forward fashion through the heart and into the inferior vena cava. Injection of contrast material revealed a thrombus in that

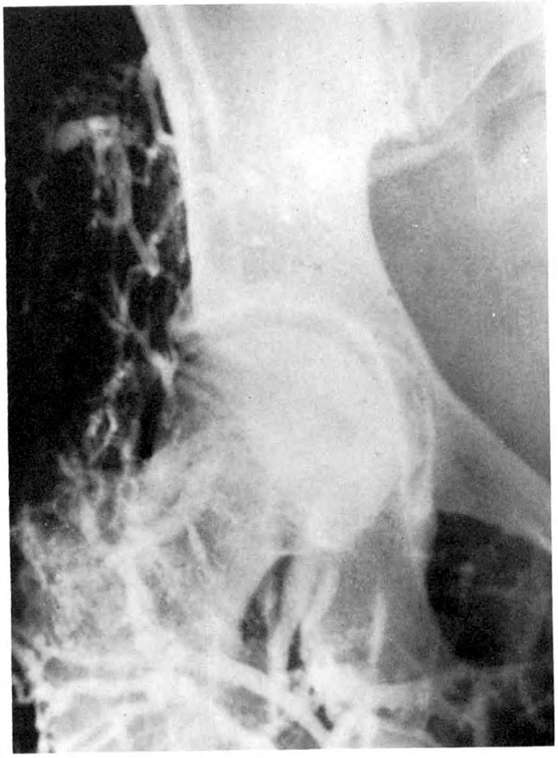

FIG. 3. Right intertrochanteric injection showing multiple abnormal collateral vessels with slight opacification of the proximal iliac vein.

vessel, measuring 8×1.5 cm., at the level of the renal veins. Additionally, complete occlusion of the left iliac vein and partial occlusion of the right iliac vein were seen (Fig. 5).

At surgery, the inferior vena cava was plicated just above the iliac veins. There were multiple collateral vessels, similar to varices, on the right renal pelvis draining towards the vena cava above the thrombus. Upon opening the vena cava, a completely fibrotic thrombus with marked extension into the right renal vein and partial occlusion of the left renal vein was found. The thrombus was easily removed and good venous flow was observed bilaterally before the vena cava was closed.

Postoperatively, the patient lost large amounts of protein, varying from 10 to 20 gm. per day, in the urine. This slowly subsided and on discharge the 24 hour urine protein loss was 3.9 gm.

Since leaving the hospital, the patient has improved considerably. She now leads an active life, although she continues to lose excessive amounts of protein. The presence of irreversible membranous glomerulonephritis makes it unlikely that she will ever return to total normality.

DISCUSSION

The multiple techniques of inferior vena cavography by way of the femoral vein have been well documented elsewhere.[4,6,9] Our usual procedure is unilateral percutaneous injection of a femoral vein by a regular 18 gauge hypodermic needle. We have not found it necessary to use a catheter. A blood pressure cuff is usually placed on the opposite leg. Multiple roentgenograms have not been required. Usually, one anteroposterior lumbar-spine-technique roentgenogram is obtained at the end of the injection of 25 cc. of contrast material.

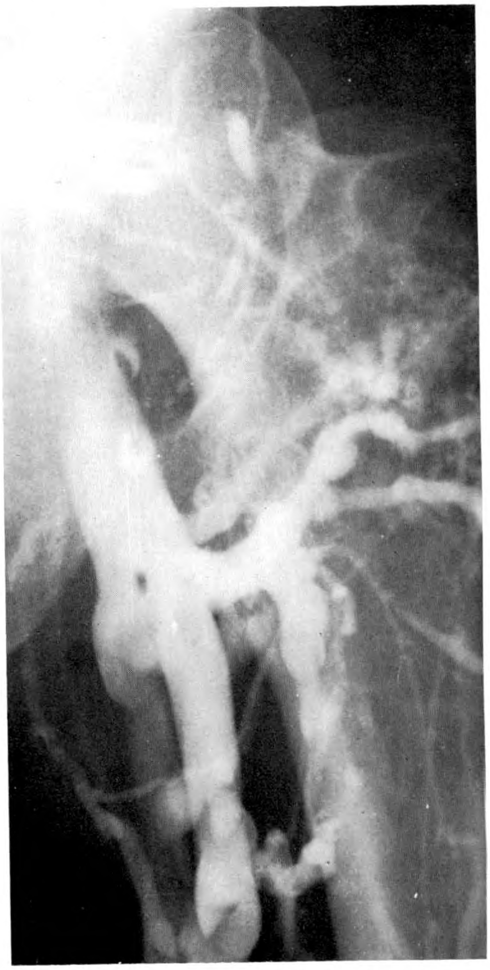

FIG. 4. Left intertrochanteric injection showing a dilated femoral vein and many abnormal collaterals.

Occasionally, this is supplemented by an oblique roentgenogram following a second injection. We make our exposure during quiet respiration; the Valsalva maneuver has been found confusing when used. We have purposely kept our technique as basic and simple as possible, both to conserve the radiologist's time and to ensure that it can be used in the absence of special skills or equipment.

In those cases in which it has been impossible to perform a suitable direct femoral vein puncture, as in markedly edematous upper thighs or for other technical reasons, we have used the intraosseous technique.[10] Following infiltration of the soft tissue structures over the prominence of the greater tuberosity, an 18 gauge regular spinal needle is inserted with a rotary motion into the marrow space of the femur. We have found it necessary to do bilateral injections in these cases. Following successful marrow puncture, 25 cc. of contrast material is rapidly injected on each side, and a single roentgenogram is made. This procedure has not proved unduly painful for the patient, or time-consuming for the radiologist, and we have been pleased with our study of the deep pelvic veins and the inferior vena cava.

In those cases where a thrombus is present in the inferior vena cava, the flow of contrast material into the vessel may be obstructed by back pressure in the iliac veins. It is then necessary to study the inferior vena cava from above. A teflon catheter is inserted into the basilic vein of the arm (it is important to use the basilic rather than the cephalic vein since it will be easier to enter the axillary vein) and threaded in forward fashion into the superior vena cava. Under constant cardiac monitoring, the catheter can easily be passed through the right atrium into the inferior vena cava. We always try to place the tip of the catheter just beyond the atrial opening for fear of dislodging possible clot. A hand injection of 25 cc. of contrast material is usually adequate to outline the inferior vena cava.

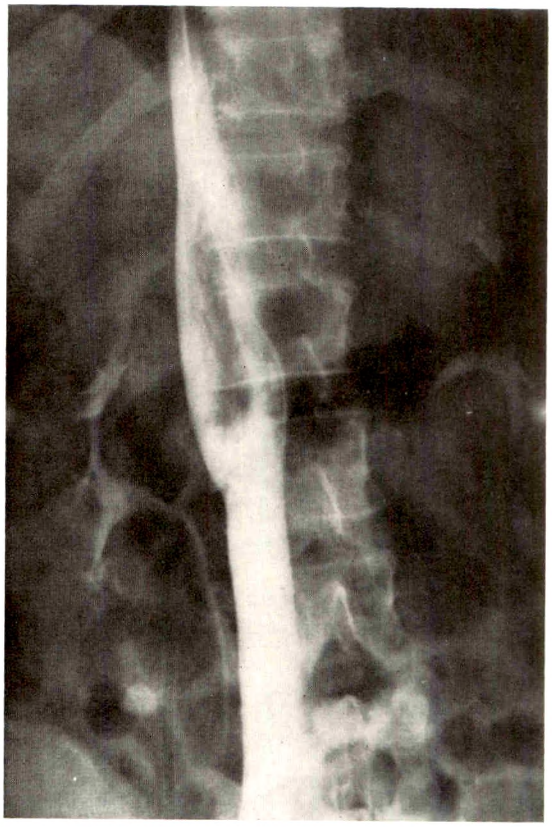

Fig. 5. A filling defect, 8×1.5 cm., in the inferior vena cava opposite the renal veins. The left iliac vein is completely occluded, while the right is partially occluded. The catheter has slipped inferiorly beyond the thrombus.

Two other methods of renal vein opacification should be mentioned. It is possible to pass a catheter up the inferior vena cava and selectively catheterize each renal vein.[8] However, since the nephrotic syndrome secondary to renal vein thrombosis is usually associated with clot in the inferior vena cava, this procedure is thought to be unnecessary and unduly dangerous. It is important also to be wary of dislodging thrombus, if present. A technique of percutaneous renal vein opacification has recently been described.[2] This is still in the experimental stage, and we have no personal experience with it.

SUMMARY

A case of nephrotic syndrome secondary to renal vein thrombosis is reported.

Three techniques of inferior vena cavography—direct femoral vein puncture, catheterization of the vena cava from above, and bilateral intertrochanteric injections—are described.

It is emphasized that an alert radiologist with a minimum of special skills or equipment can play a crucial role in clarifying the etiology of the nephrotic syndrome in selected cases.

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EARLY FORMS OF RENAL PAPILLARY NECROSIS*

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IN A previous paper[3] extensive forms of renal papillary necrosis from analgesic abuse and from diabetes were described and illustrations of the medullary and the papillary types were presented. However, an earlier form of renal papillary necrosis can also be identified with considerable confidence in a great number of patients, especially those with diabetes mellitus. We have found an incidence of 18 per cent (9 out of 50) in patients with long standing diabetes.[4] The increased incidence over that reported in the past literature is due to an awareness of the pathology and to the use of double doses of contrast agent with marked abdominal compression during intravenous urography.[5]

ILLUSTRATIVE CASES

CASE I. An elderly diabetic woman developed left flank pain and pyuria with bacteriuria. Roentgenograms showed a ring-shaped calculus with a nonopaque center which proved to be a stone in the pelvis of the left kidney. A retrograde pyelogram revealed the pelvic stone and, in addition, small cavities typical of the medullary form of renal papillary necrosis. A left pyelolithotomy was done with an uneventful postoperative course. Sections of the stone disclosed the nonopaque center to be a sloughed papilla which undoubtedly arose from the elongated cavity extending from the upper calyx. Despite the large size of the sloughed papilla, the roentgenographic findings in regard to the calyces were not extensive.

CASE II. An elderly diabetic woman developed bilateral flank pain, pyuria and early azotemia. On a roentgenogram of the kidney, ureter and bladder, 4 small ring-shaped calcifications were identified (Fig. 1*A*). An intravenous urogram without compression demonstrated the calcifications to be at the apices of the pyramids (Fig. 1*B*). Moreover, the calyceal fornices were intact, but contrast agent surrounded each calcification. The findings represented a medullary form of renal papillary necrosis with sloughed portions of necrotic papillae which remained in place and upon which calcium salts had been deposited.

CASES III and IV. Both patients were middle aged women with mild diabetes of about 8 years' duration. The only symptoms were occasional frequency and dysuria due to a cystitis which was readily cured on antimicrobial therapy. Case III (Fig. 2) demonstrated cavities in the right kidney in the pyramids at the tip of every calyx. Case IV showed 3 similar medullary cavities. Both cases are considered a medullary form of renal papillary necrosis since the calyceal fornices were intact.

CASE V. A 23 year old woman with juvenile diabetes of 12 years' duration developed upper urinary tract infection which was controlled with difficulty by using large doses of antibiotics. Intravenous urograms demonstrated minute cavities of medullary renal papillary necrosis, representing about the earliest form of renal papillary necrosis that can be diagnosed roentgenographically.

CASE VI. A 23 year old woman had mild diabetes for several years. Because of one episode of pyuria, which was easily controlled on therapy, intravenous urography was performed (Fig. 3*A*). A papillary form of renal necrosis was seen in the upper calyx. The cavity was larger than expected in the oblique view (Fig. 3*B*).

CASE VII. A middle aged woman with mild diabetes and mild recurrent cystitis developed destruction of all the fornices, representing an early form of renal papillary necrosis (Fig. 4).

CASE VIII. A middle aged diabetic man experienced sudden severe left renal colic. At cystoscopy a piece of tissue was recovered from the opening of the left ureter which showed a necrotic papilla on histologic sections. A retrograde pyelogram demonstrated a more advanced papillary necrosis with destruction of the fornices of all calyces and also several ring forms.

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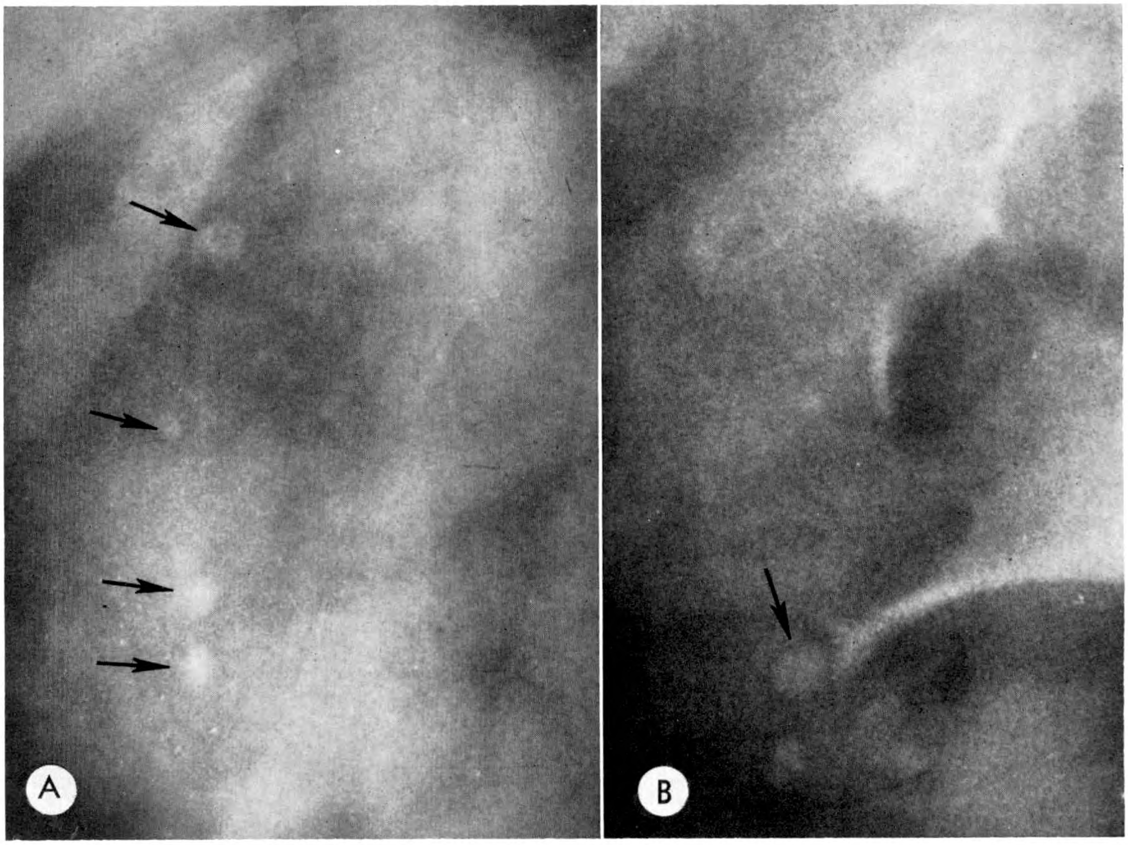

Fig. 1. Case ii. (*A*) Arrows point to 4 small ring-shaped calcifications in the left kidney of a diabetic patient. (*B*) An excretory urogram shows contrast agent surrounding each calcification, proving that the nonopaque centers are sloughed medullary tissue which have become calcified. An arrow points to one calcification which illustrates best the relationship to the calyx.

DISCUSSION

Only Case i and Case viii were proven histologically, but the clinical and roentgenographic findings in the other cases also strongly suggest the diagnosis of renal papillary necrosis. In the past, papillary necrosis was considered a rapidly fatal disease in most instances; yet, in our experience as well as in that recently reported by others,[7] most cases progress slowly or not at all. It is probable that many of these relatively early cases were not diagnosed properly and it should be noted that all except i of our patients were thought to have pyelonephritis by the initial examiner.

Diagnosis has become of more than academic interest for several reasons. In diabetes, the physician is alerted to the fact that more prolonged antimicrobial therapy and more careful evaluation of bacteriuria will be required. By good care, many useful lives can be considerably prolonged. Most evidence indicates that the infection is superimposed on the papillary necrosis rather than *vice versa*, but control of infection prevents rapid deterioration of renal function.

In the abusers of analgesics, the withdrawal of the phenacetin-containing compounds may arrest further renal damage. The evidence, however, is not conclusive that phenacetin alone causes the damage.[6] Some authorities have suggested that salicylates or other anti-inflammatory compounds may also be incriminated,[2] and many cases of renal papillary necrosis occur in patients without diabetes or even excess phenacetin intake. Recognition of these cases from roentgenographic studies may lead to discovery of other lesions or other drugs as causes of the necrosis. In observations that are to be published, I have been unable to validate ureteral obstruction as a sole factor in papillary necrosis in humans.

PROGRESSION OF LESIONS

Some cases have been encountered where rapid changes led to a conclusive diagnosis of renal papillary necrosis. Figure 5*A* shows a ring shadow in the upper calyx of a patient who overused phenacetin compounds. One and one-half years later an excretory urogram showed that the pyramid had sloughed away (Fig. 5*B*). In another abuser of analgesics, an early urogram revealed normal calyces (Fig. 6*A*), but 2 years later extensive papillary necrosis was evident on a retrograde pyelogram (Fig. 6*B*). In a 48 year old diabetic wom-

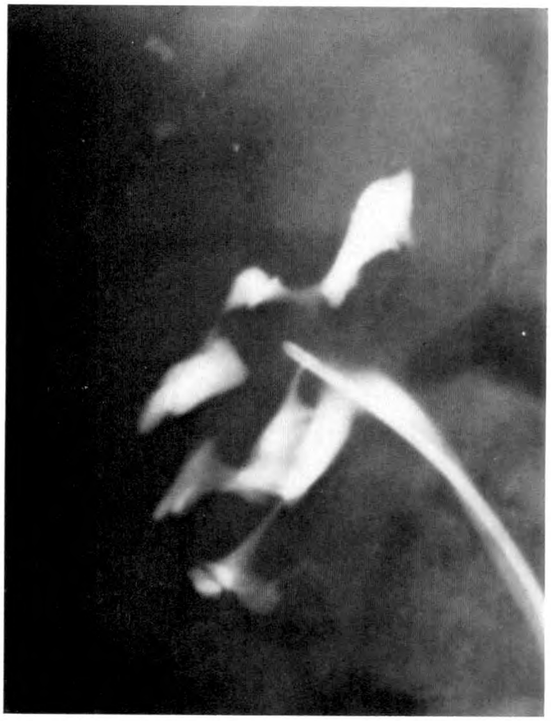

FIG. 2. Case III. Every pyramid has a cavity separated by 1 or 2 mm. from the calyx. Medullary form of renal papillary necrosis.

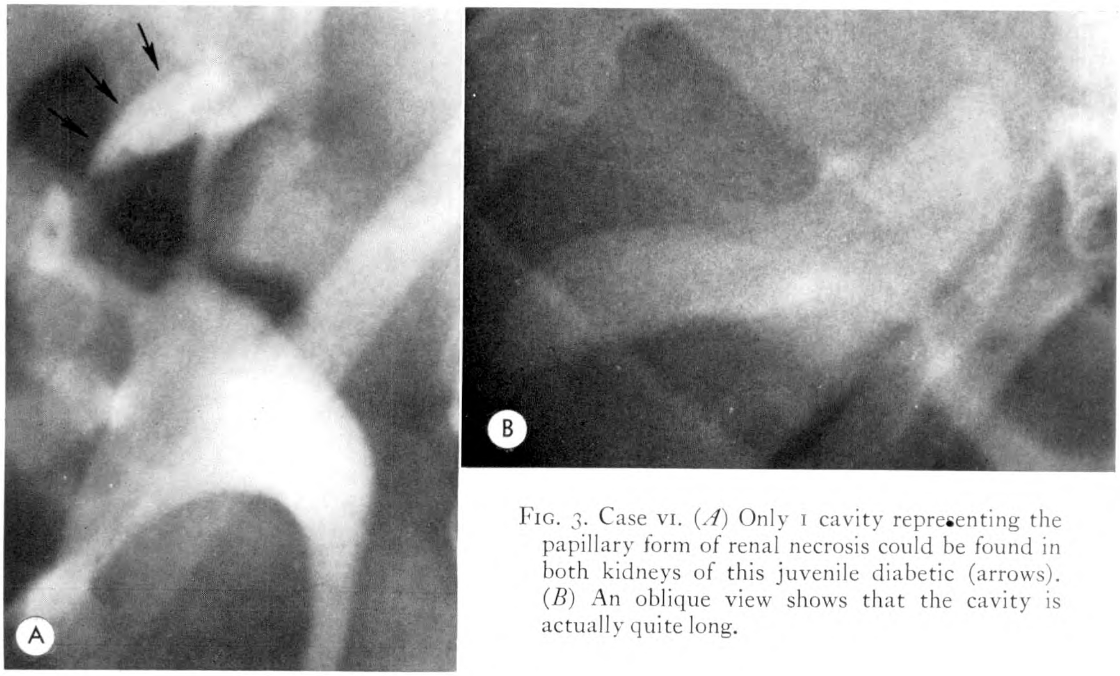

FIG. 3. Case VI. (*A*) Only 1 cavity representing the papillary form of renal necrosis could be found in both kidneys of this juvenile diabetic (arrows). (*B*) An oblique view shows that the cavity is actually quite long.

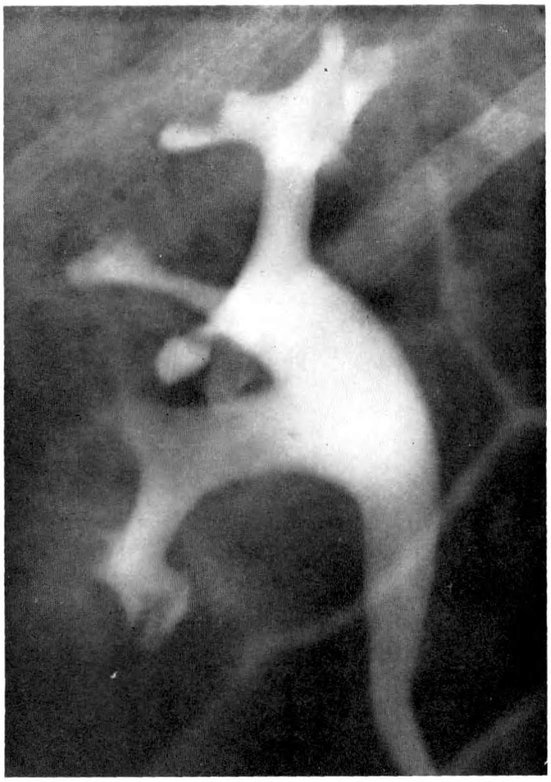

FIG. 4. Case VII. Papillary form of renal necrosis is seen with destroyed fornices of the calyces.

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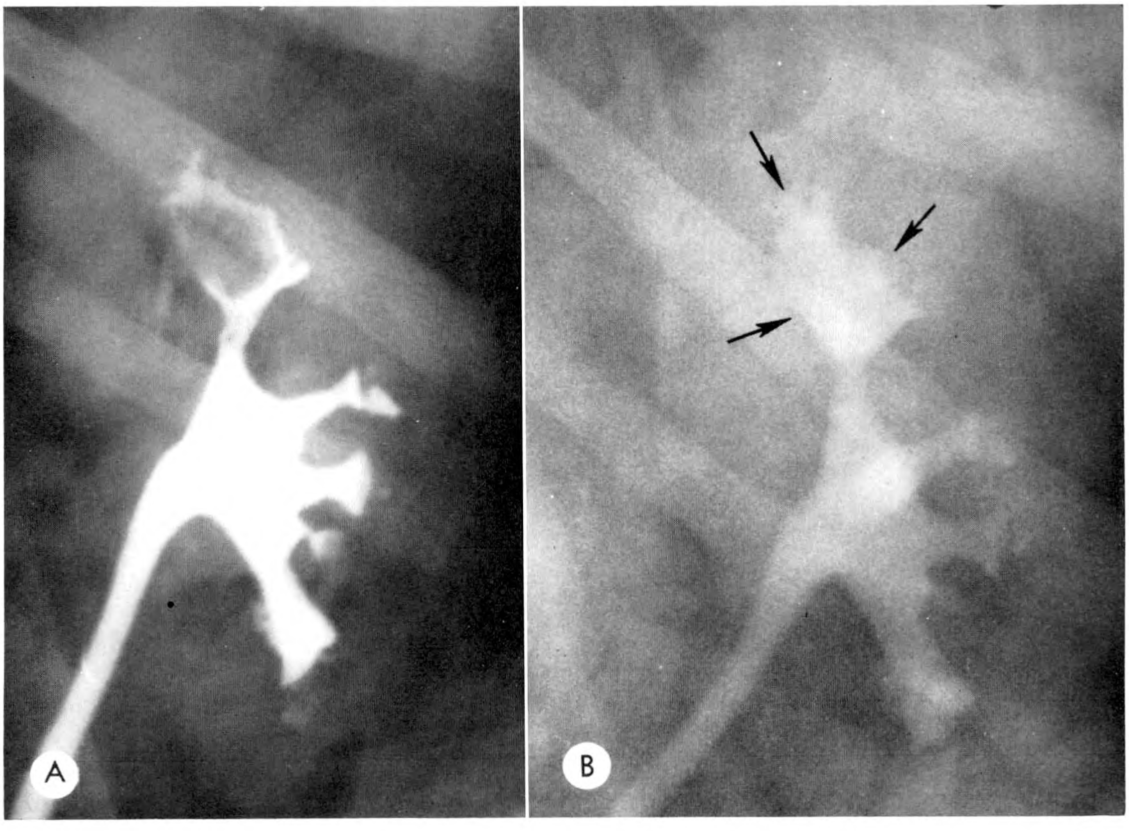
an, an intravenous pyelogram revealed no unusual findings (Fig. 7*A*). One year later a left retrograde pyelogram revealed renal papillary necrosis with 3 large filling defects in the upper pyramids (Fig. 7*B*). Several weeks later the papillae had sloughed and passed spontaneously leaving 3 cavities (Fig. 7*C*). The clinical history of these 3 patients has been reported previously,[3] without showing the roentgenographically demonstrable progression of the lesions.

In a different situation, 2 nondiabetic middle aged women who denied overuse of any drugs passed fragments of tissue spontaneously which histologically proved to be necrotic papillae. Yet, at the time of pas-



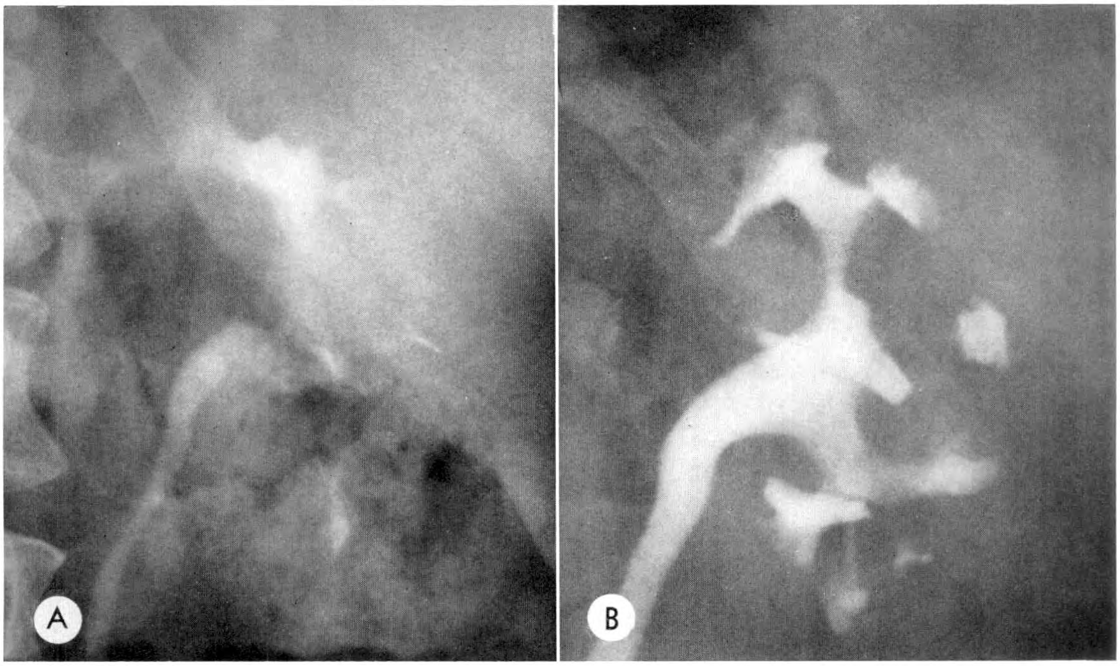


Fig. 6. (*A*) An intravenous pyelogram without compression faintly demonstrates normal calyces. (*B*) Two years later this patient who overindulged in analgesics demonstrates typical renal papillary necrosis in every calyx.

sage of rather large chunks of tissue, excretory urograms and retrograde pyelograms were normal (Fig. 8*A*). In 1 of these patients, a repeat right retrograde study 4 months later showed renal papillary necrosis for the first time (Fig. 8*B*). On a repeat left retrograde study, the second patient also demonstrated severe papillary necrosis (Fig. 8*C*).

DIFFERENTIAL DIAGNOSIS

Pyelorenal backflow, calyceal diverticula, pyelogenic cysts, neoplasms, blood clots and ordinary stones can almost always be differentiated from renal papillary necrosis by careful examinations. Renal dysplasia superficially resembles renal papillary necrosis, but the calyces usually project much further into the cortex.[1] Figure 9, *A* and *B* shows a right-sided renal dysplasia in a 24 year old woman without previous urinary tract infections or ureteral reflux; this is probably a congenital form of dysplasia. In Figure 10, *A* and *B*, 2 different types of true sponge kidneys are demonstrated which can hardly be confused with renal papillary necrosis. We have encountered 12 patients with considerable dilatation of the ducts of Bellini diagnosed by others as sponge kidneys but probably representing congenitally dilated ducts without actual cyst formation. Moreover, ability to concentrate

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Fig. 5. (*A*) Large semicircular tracts in the upper calyx represent papillary renal necrosis involving the entire pyramid. Medullary forms can be identified in the other calyces. (*B*) Eighteen months later an excretory urogram shows that the upper pyramid has sloughed leaving a large cavity (arrows). A double dose of contrast agent and abdominal compression were used because of hyposthenuria. The patient was an abuser of phenacetin. (*A* is reproduced with permission from *J.A.M.A.*, 1963, *184*, 445–452.[3])

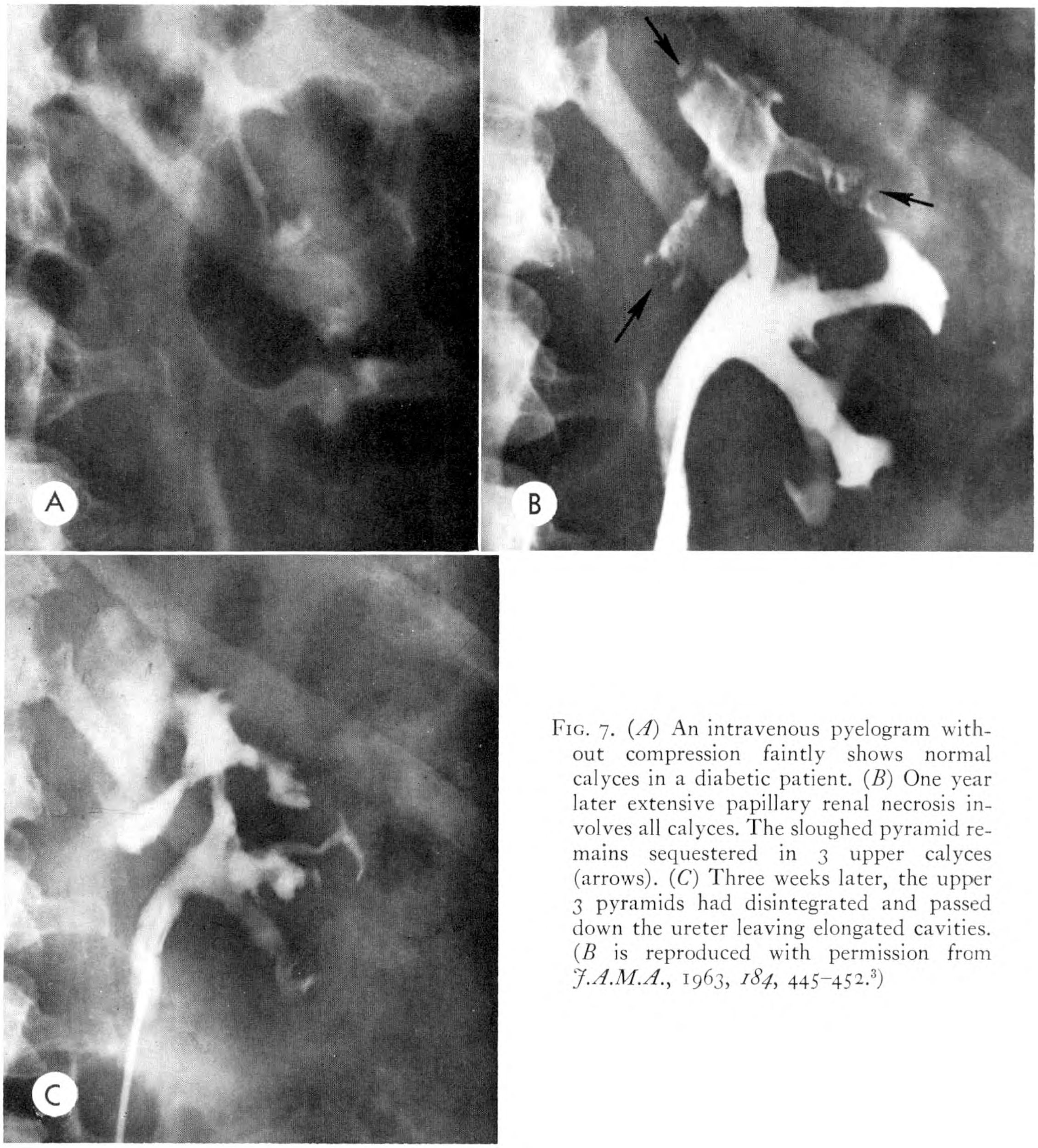

FIG. 7. (*A*) An intravenous pyelogram without compression faintly shows normal calyces in a diabetic patient. (*B*) One year later extensive papillary renal necrosis involves all calyces. The sloughed pyramid remains sequestered in 3 upper calyces (arrows). (*C*) Three weeks later, the upper 3 pyramids had disintegrated and passed down the ureter leaving elongated cavities. (*B* is reproduced with permission from *J.A.M.A.*, 1963, *184*, 445-452.[3])

the urine was not impaired in these instances.

Tuberculosis can mimic renal papillary necrosis almost exactly. Figure 11*A* shows a form which appears identical to renal papillary necrosis but cultures revealed tuberculosis. Figure 11*B* shows a more mottled and irregular appearance than that in renal papillary necrosis and again cultures revealed tuberculosis. In general, the marked irregularities, the infundibular and ureteral strictures, and the bacteriologic identification will enable a diagnosis to be made.

Chronic pyelonephritis, especially in the later stages, is most apt to be confused with renal papillary necrosis. Only if serial pyelograms are obtained or sloughed papillae are recovered by straining the urine or by cystoscopic removal can a definite diagnosis be made.

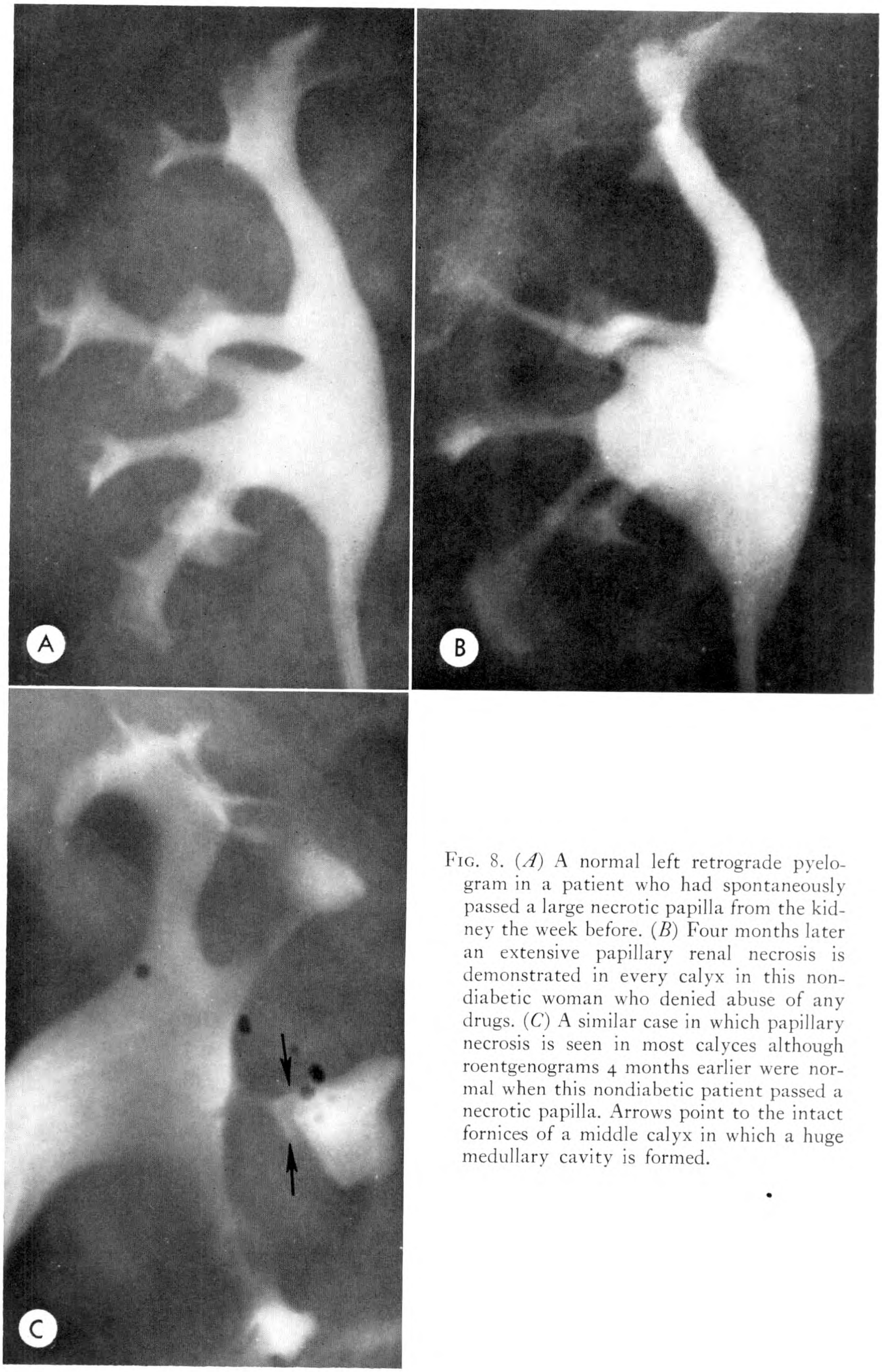

FIG. 8. (*A*) A normal left retrograde pyelogram in a patient who had spontaneously passed a large necrotic papilla from the kidney the week before. (*B*) Four months later an extensive papillary renal necrosis is demonstrated in every calyx in this nondiabetic woman who denied abuse of any drugs. (*C*) A similar case in which papillary necrosis is seen in most calyces although roentgenograms 4 months earlier were normal when this nondiabetic patient passed a necrotic papilla. Arrows point to the intact fornices of a middle calyx in which a huge medullary cavity is formed.

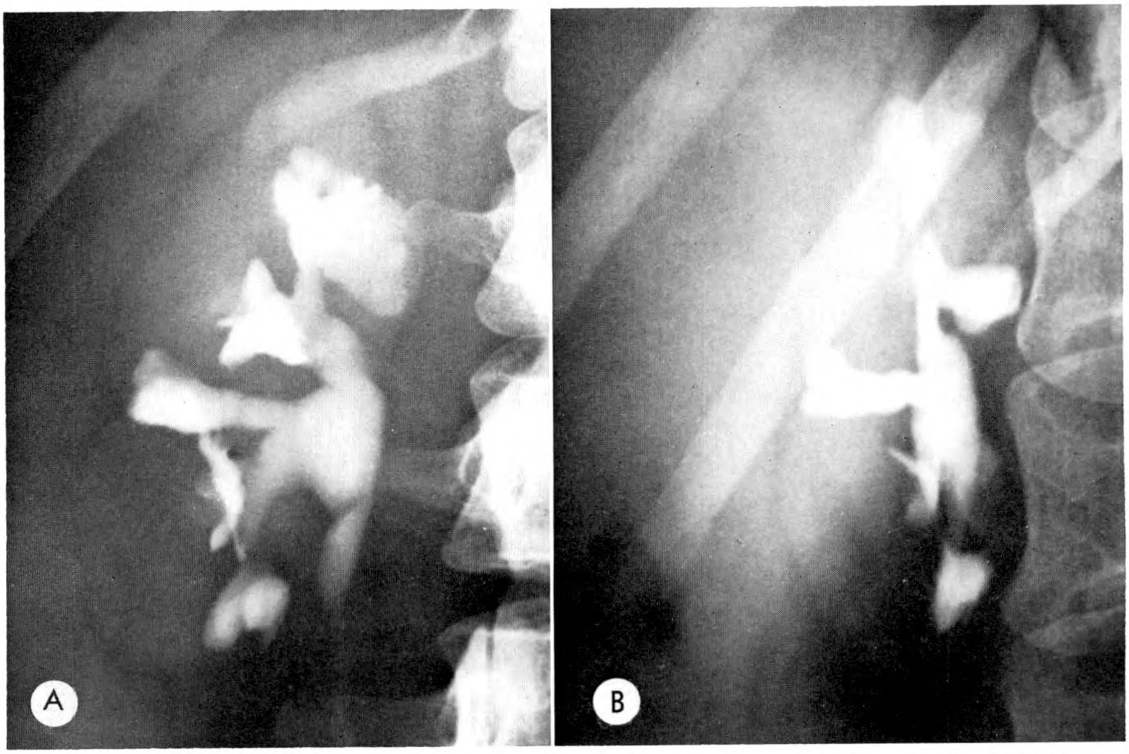

FIG. 9. (*A*) An anteroposterior view shows a congenital dysplastic kidney with calyces projecting deep into the cortex in a woman without pyelonephritis or ureteral reflux. (*B*) An oblique view of the same dysplastic kidney.

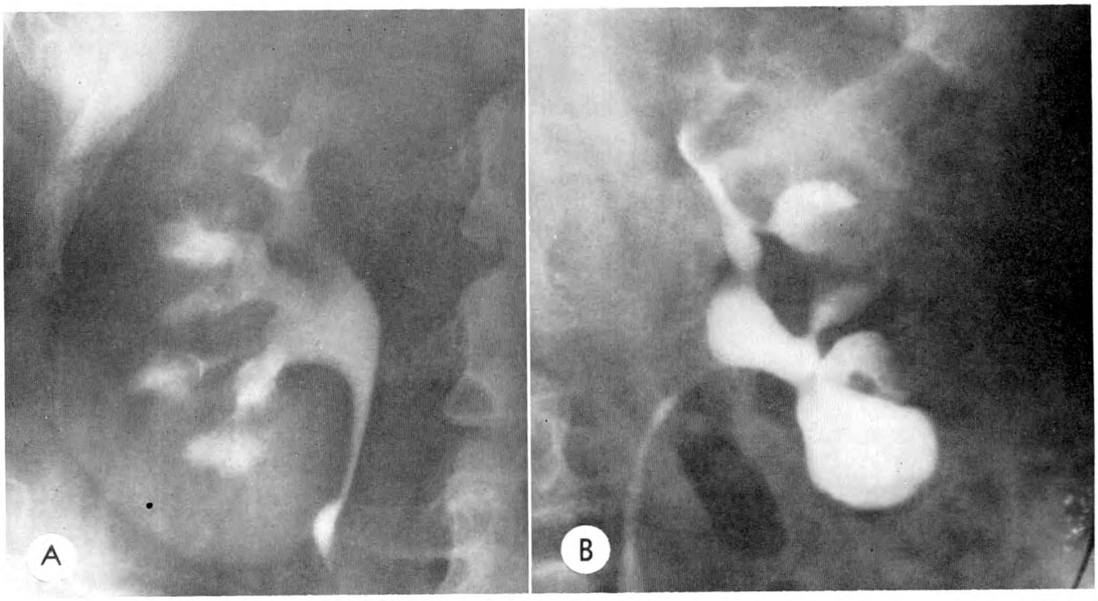

FIG. 10. (*A*) A type of sponge kidney which should not be confused with renal papillary necrosis. (*B*) A sponge kidney with large communicating cysts without any resemblance to renal papillary necrosis.

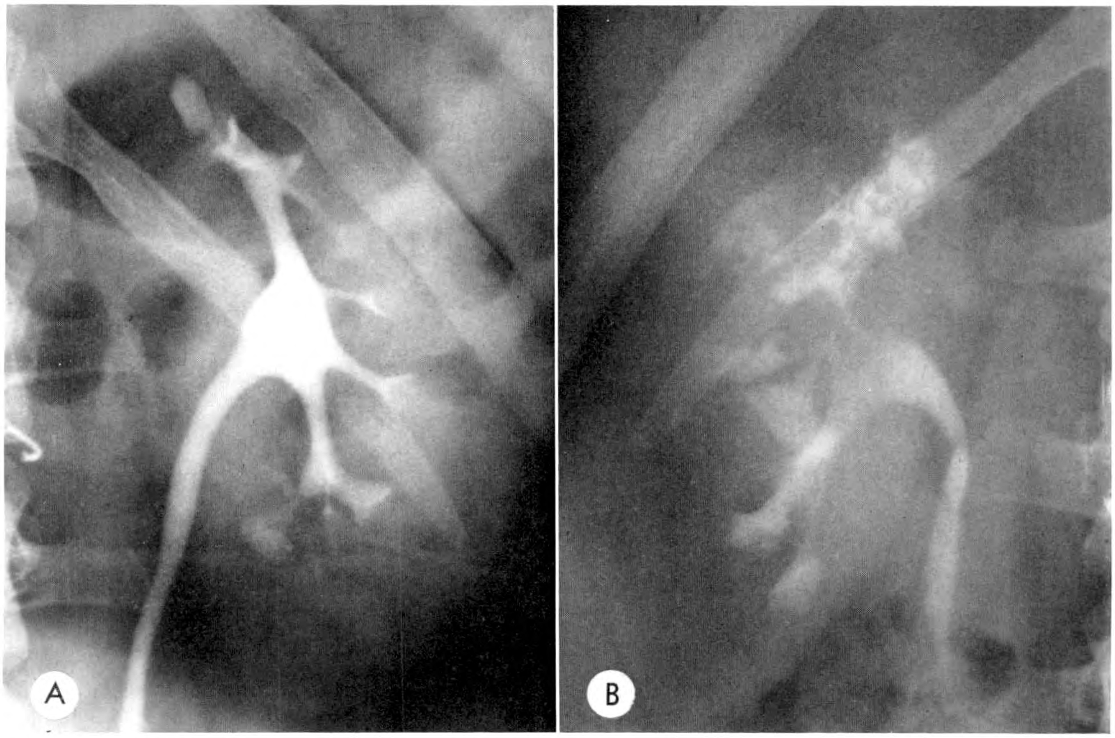

Fig. 11. (*A*) A case of proven tuberculosis of the kidney which mimics renal papillary necrosis exactly in regard to the roentgenographic pattern. (*B*) Another example of tuberculosis that resembles renal papillary necrosis but the pattern is too irregular.

SUMMARY

Cases are presented to show that early forms of renal papillary necrosis can be confidently recognized. In patients having long-standing diabetes, the incidence of renal papillary necrosis was 18 per cent. Identification is important for directing proper treatment and for the search of unknown etiologies of renal papillary necrosis in patients without diabetes, analgesic abuse or urinary tract obstruction. Late stages of renal papillary necrosis may not be distinguished in many instances from chronic pyelonephritis unless fragments of necrotic tissue have been recovered. In 2 patients who passed necrotic papillae, initial retrograde pyelograms were normal.

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CORTICAL CALCIFICATION IN RENAL CORTICAL NECROSIS

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SURVIVAL of the acute episode of bilateral renal cortical necrosis may produce roentgen signs which are characteristic in appearance and location. Roentgenologic demonstration of a rim of cortical calcification located at the periphery of the renal shadows with evidence of contracted kidneys and accompanied by a hemorrhagic complication of late pregnancy has been previously reported as being diagnostic of renal cortical necrosis.[13,14]

Since the original description by Juhel-Renoy[11] in 1886, sporadic cases of renal cortical necrosis which survived the acute episode have been reported.[8,9,12,20] To our knowledge, only 7 cases have been reported where antemortem renal cortical calification was demonstrated by roentgen means.[1,5,10,13,14,15,18] The authors wish to present a case of renal cortical necrosis with over a 2½ year survival period following the acute episode in which the above mentioned signs were demonstrated. The case is considered of interest because autopsy findings correlated with the anatomic, pathologic, and roentgenologic studies of the disease process.

REPORT OF A CASE

S.D., a 30 year old married Caucasian female, gravida 5, para 1, was hospitalized on October 18, 1960 with complaints of nausea, backache and vaginal spotting. Her last mentrual period was on May 5, 1960.

Past medical history revealed that with her first pregnancy in 1950, the patient delivered a stillborn fetus at 36 weeks' gestation. She was reported to have had minimal signs of toxemia and a kidney infection with this pregnancy. Her only living child was born in 1952 following what was described as a normal pregnancy. In 1951 and 1960 spontaneous abortions occurred at approximately 12 weeks' gestation. The patient reported having had an elevated blood pressure since her first pregnancy. When hospitalized in May, 1958 for an appendectomy and in November, 1959 for a tonsillectomy, the recorded blood pressures were 150/90 and 170/90, respectively. On each occasion urinalysis was negative with a specific gravity of 1.020.

On physical examination, the patient was 5 months pregnant. Generalized back pain was present without localized costovertebral angle tenderness. The blood pressure was 180/120. Arteriolar constriction was noted bilaterally on funduscopic examination. On the day following admission, a stillborn fetus was delivered. Marked oliguria became apparent the same day with a total urine output at 40 cc./24 hours. There was 1+ proteinuria, with 15–20 white blood cells and 150 red blood cells per high power field. The blood urea nitrogen was 40 mg. per cent. During the subsequent 2 days the urine output dropped to 7 cc./24 hours. On the fourth day the patient was transferred to the University of Minnesota Hospitals for possible hemodialysis.

Examination on admission showed marked bilateral costovertebral angle tenderness. Edema was generalized but most pronounced in the face, hands and feet. The blood pressure was 150/90. Urinalysis showed 2+ proteinuria with 8–30 red blood cells and 20–50 white blood cells per high power field. The urine output was 16 cc./24 hours. The hemoglobin was 7.7 gm. and the white blood cell count 10,500 with 88 per cent neutrophils. The blood urea nitrogen was 93 mg. per cent and rose to 158 mg. per cent 2 days later. On the seventh day of oliguria a 6 hour hemodialysis on the Kolff artificial kidney lowered the blood urea nitrogen to 67 mg. per cent. Cystoscopy and retrograde pyelography on the ninth day showed no obstruction. The renal shadows were normal in size and position and there was no calcification.

During the week following hemodialysis, the

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blood urea nitrogen gradually rose to 152 mg. per cent. The urine output increased from 66 cc. the day following hemodialysis to 820 cc. 7 days later. The blood urea nitrogen gradually decreased when the urine output consistently exceeded 1,000 cc./24 hours. This started about 10 days after hemodialysis. The specific gravity was 1.005 with 1+ proteinuria. Urine culture grew out more than 100,000 colonies/cc. of *E. coli* and became sterile following treatment. The patient was discharged on December 3, 1960 with a blood urea nitrogen of 77 mg. per cent, a urine output greater than 2,000 cc./24 hours and a blood pressure of 144/96.

She was re-admitted to the University Hospitals on January 25, 1961. The blood pressure was 188/136 and the blood urea nitrogen 64 mg. per cent. There was 1+ proteinuria and urine cultures again grew out more than 100,000 colonies/cc. of *E. coli.* A urine concentration test revealed a maximum specific gravity of 1.009. On February 6, 1961 cystoscopy and bilateral retrograde pyelography were repeated. The preliminary roentgenogram (Fig. 1) showed that the renal shadows were normal in position but contracted. Dense cortical calcification with accentuation of the margins was symmetrically present. The collecting systems were normal with no obstructive uropathy. The urine output during the admission ranged from 2,000 to 3,000 cc./day. Cultures became sterile on antibiotic therapy and she was discharged on antihypertensive medication.

In June and August, 1961 she was treated in the out-patient department as urinary cultures grew out more than 100,000 colonies/cc. of alpha streptococcus. Her blood pressure ranged from 140/100 to 160/110. She was hospitalized in January, 1962 for pneumonia and urine cultures grew out more than 100,000 colonies/cc. of alpha streptococcus. From January to June, 1963 she was hospitalized on 3 occasions. With each of these admissions, there was progressive decrease in the urine output and a rising blood urea nitrogen. On the final admission in June, 1963, the urine output was 550 cc./day and the blood urea nitrogen 238 mg. per cent. Her blood pressure was 220/100. There was no response to water loading so fluids were restricted. Coagulase positive staphylococci were cultured from the blood and urine. The patient did not respond to continuing therapy and expired on July 2, 1963 with a terminal blood urea nitrogen of 280 mg. per cent.

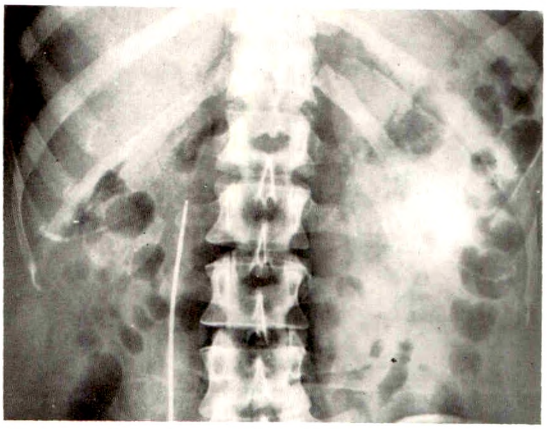

FIG. 1. Preliminary roentgenogram of the retrograde pyelogram. Accentuation of the margins of the renal shadows by cortical calcification is demonstrated in the contracted kidneys.

Gross Necropsy Findings. Both kidneys were markedly contracted. The right weighed 35 gm. and the left 65 gm. The capsules stripped with ease. The surfaces were covered with small, hard, discrete to confluent, yellow, rough excrescences resembling coarse sandpaper (Fig. 2). On section the cortex was thin, ill-defined, 1–2 mm. in thickness and contained calcific material (Fig. 3). The columns of Bertini likewise appeared thin without sharp delineation from the medulla. The medulla was not remarkable. There was no obstruction of the major arteries or veins. The renal pelves, ureters and bladder showed no gross abnormality. Other significant findings at necropsy included left pleural adhesions, a right pleural effusion of about 1,500 cc. and about 3,000 cc. of ascitic fluid. Bilateral bronchopneumonia and pulmonary edema were present. The heart was enlarged and weighed 480 gm.

Microscopic Findings. The cortex was thin with an indistinct demarcation from the medulla. In a broad subcapsular band there were nodular and confluent calcific debris and dense fibrous tissue along with an occasional entrapped island of tubular epithelium (Fig. 4). In the persistent juxtamedullary cortex a few glomeruli were present and tended to be in small groups. Some of these glomeruli appeared normal; however, the majority showed varying degrees of hyalinization. A fibrous tissue rim was noted about the glomerular capsules. There was marked loss of tubules. Some residual tubules were dilated and granular hyaline casts were present. A mild interstitial lymphocytic

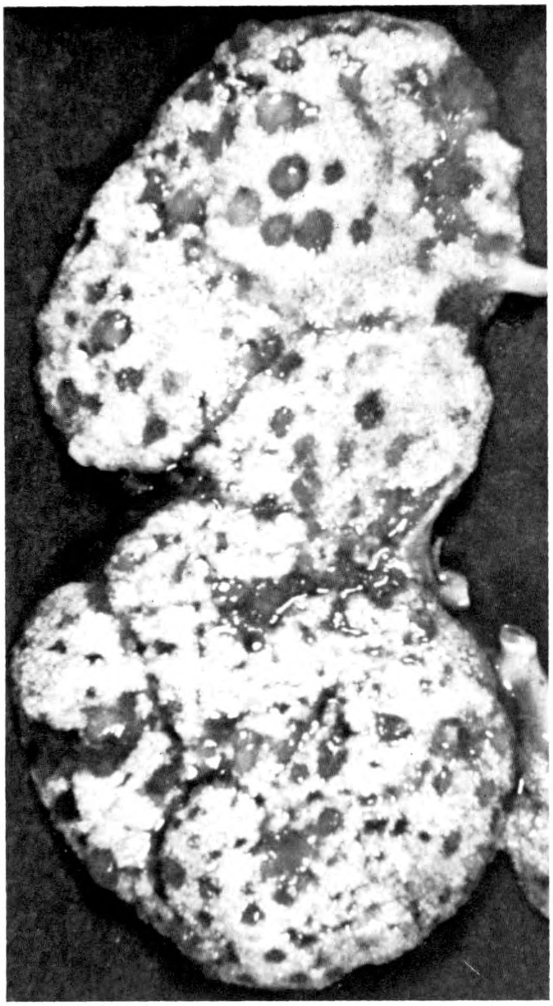

Fig. 2. Gross specimen of the right kidney. Actual size. The extensive calcification is seen as the light granular area. The small dark depressed patches are atrophic without calcification.

infiltrate was present with occasional small focal aggregates in the cortex. Scattered neutrophils were present in several tubules. Large arteries and the medium and small branches were prominent and showed fibrohyaline intimal thickening. In the small arteries and arterioles there was edematous intimal thickening with marked narrowing of the lumen. No thrombonecrosis was noted. There was no evidence of primary glomerular disease.

DISCUSSION

This condition is manifested by symmetric ischemic necrosis of the cortices of the kidneys with only a narrow rim of subcapsular tissue and the medulla being preserved. The etiology of acute symmetric renal cortical necrosis associated with a complication of pregnancy has been attributed to a sustained vascular spasm of the interlobar and intralobular arteries of the kidney followed by thrombosis and coagulation necrosis. The typical lesion of renal cortical necrosis has been produced experimentally by DeNavasquez[6] with staphylococcus toxin and by Page and Glendening[17] with serotonin. Clinically occurring renal cortical necrosis secondary to other mechanisms and toxins have been reviewed by Duff and Murray,[7] Sheehan and Moore,[19] and Phillips.[18]

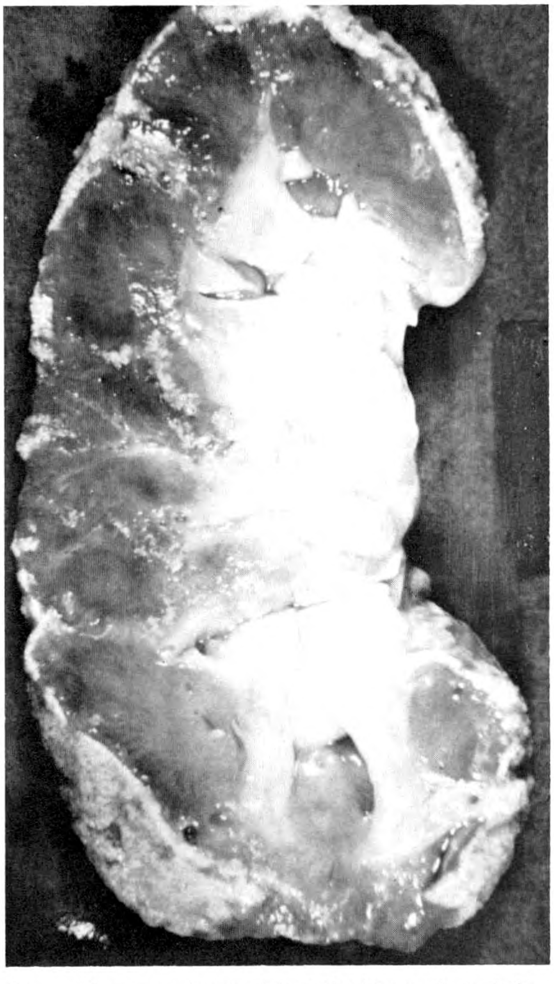

Fig. 3. Gross specimen of the left kidney. Actual size. The calcification is seen about the periphery of the thin indistinct cortex.

Renal cortical necrosis occurs most frequently in conjunction with a hemorrhagic complication of late pregnancy. As illustrated in this case, the multiple pregnancies, pre-existing hypertension, and toxemia accompanied by bilateral flank pain and acute anuria are clinical features usually manifested in this condition.

While it is apparent that no one can survive complete destruction of both renal cortices, it is likewise probably that gradations do occur from focal infarctions to complete symmetric cortical necrosis. The recorded survivors with renal cortical necrosis must fall into an intermediate category in which the diffuse symmetric necrosis spares a sufficient number of glomeruli to maintain life.

ROENTGEN FINDINGS

McAlister and Nedelman[14] reviewed the roentgen findings of renal cortical necrosis and emphasized the accentuation of the periphery of the renal shadow secondary to cortical deposition of calcium and the contraction of the kidneys bilaterally. It must be stressed that detection of the presence of renal calcification, which may appear as early as 30 days following the acute episode, may be possible only by utilizing laminagraphy of the kidneys. Calcification of the cortex similar to that seen in renal cortical necrosis has been described in only one other disease process. Vaughn, Sosman, and Kinney,[21] in 1947, reported a case of chronic glomerulonephritis in which deposition of calcium, mainly confined to the cortex, was associated with a generalized increase in density of the renal shadows. Subsequently, Arons, Christensen and Sosman[2] described 4 additional cases of chronic glomerulonephritis in which cortical calcification was roentgenologically demonstrated and confirmed at necropsy. Correlation with history should aid in differentiating the above from renal cortical necrosis.

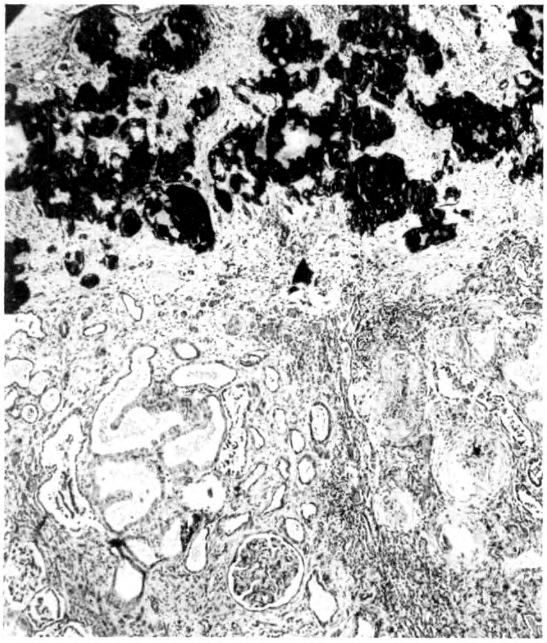

FIG. 4. Histologic section of the cortex (H & E, ×40). The cortical surface is visible in the left upper corner. The dark staining calcific material lies in the immediate subcapsular zone. A normal glomerulus is present.

SUMMARY

A case of bilateral renal cortical necrosis is reported with over a $2\frac{1}{2}$ year survival period following the acute episode. The characteristic rim of cortical calcification, detectable by roentgen examination is demonstrated. The cortical calcification is correlated with the pathologic findings in the disease process.

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RENAL ANGIOGRAPHY IN PYELONEPHRITIS, GLOMERULONEPHRITIS, AND ARTERIOLAR NEPHROSCLEROSIS*

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IN VIVO angiography has made possible more precise study of renal vascular and parenchymal disease. The arterial, nephrographic, and venous phases during angiography of the normal kidney have been described in detail.[2,5,8] The findings during renal arteriography have been reported in congenital ectopia,[5,22] benign cyst,[5,8,26] malignant tumors of the cortex[5,6,8,22,26] or pelvis[5], hydronephrosis,[3,5,14,22,26] tuberculosis,[7,26] polycystic disease,[1,5,22,26] arteriovenous malformations,[5] trauma,[12,21] calculus disease[8] and renal artery embolus[10,23] and stenosis.[5,11,19] The purpose of the present authors is to describe the findings during renal angiography in patients with pyelonephritis, glomerulonephritis, and arteriolar nephrosclerosis.

MATERIAL AND METHODS

The clinical, roentgenographic, and available pathologic data were reviewed in 12 patients with pyelonephritis, 4 with glomerulonephritis, and 3 with arteriolar nephrosclerosis (Table I). All patients had aortography for evaluation of the renal arteries and kidneys. Diagnoses were confirmed histologically in 8 patients with pyelonephritis, 3 with glomerulonephritis, and 3 with arteriolar nephrosclerosis (3 autopsy, 7 nephrectomy, 2 open biopsy, and 2 needle biopsy). The 5 patients without histologic proof of the nature of their renal disease were included because their clinical and more routine roentgenographic findings were typical of either pyelonephritis or glomerulonephritis. Ages of the patients ranged from 7 to 71 years; 6 were males and 13 were females; 17 were Caucasian and 2 were Negro.

Aortography was performed under 1 per cent lidocaine hydrochloride* local anesthesia by percutaneous transfemoral introduction of a yellow or gray Ödman-Ledin catheter,† using the Seldinger technique.[24] The tip of the catheter was positioned fluoroscopically at the inferior cortical margin of T12. Contrast material was 60 per cent methylglucamine diatrizoate,‡ 60 per cent meglumine iothalmate,§ or 75 per cent sodium diatrizoate.‖ Fifteen to 30 milliliters were injected in children and 30–60 milliliters in adults, scaled according to the size of the patient. The Gidlund or Cordis automatic injector was used with 4–7 kg./cm.² or 300–500 psi pressure, respectively, in order to deliver approximately 25 ml. of contrast material per second. Fifteen 14 by 14 inch films were exposed with the Schönander film changer at a rate of 3 films per second for 10 films and then 1 film every other second for 5 films. The injection was begun after the patient had been straining against the closed glottis for at least 10 seconds, and the Valsalva maneuver was released after exposure of the first 10 films. Angiography produced no detectable untoward effect upon the kidneys; no complications resulted from the examinations.

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* Xylocaine hydrochloride, Astra Pharmaceutical Products, Inc., Neponset Street, Worchester 6, Massachusetts.

† A. B. Kifa Company, Stockholm, Sweden.

‡ Renografin, E. R. Squibb and Sons, 745 Fifth Avenue, New York 23, New York.

§ Conray, Mallinckrodt Pharmaceuticals, Mallinckrodt Chemical Works, St. Louis 7, Missouri.

‖ Hypaque, Winthrop Laboratories, 1450 Broadway, New York 18, New York.

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TABLE I

SUMMARY OF ABNORMAL FINDINGS

Clinical, Laboratory, and Pathologic Data	Roentgenographic Findings
Pyelonephritis	
1. C.S., white female, aged 35 years. Recurrent urinary tract infections for 7 years with intermittent right flank pain, chills, and fever. BSA 1.36 m.^{2}. 120/80. Urinalysis: 6–7 wbc/hpf, 4+bacteria. Urine culture: heavy growth of *E. coli*. Right nephrectomy (Nov. 1, 1963): chronic pyelonephritis (broad scars involving whole cortex).	Bilateral asymmetry. Right only involved. Intravenous urogram and retrograde pyelogram (Oct. 26, 1963): right kidney 11.5×5 cm.; left kidney 14.3×5.8 cm.; marked caliectasis right kidney. Cystography: right ureteral reflux. Renal angiogram (Oct. 29, 1963): decreased caliber of right renal artery; inhomogeneous right nephrogram with decreased cortical width and localized areas of marked cortical atrophy.
2. L.B., white female, aged 34 years. Pregnancies 15 and 14 years ago complicated by edema. Hypertension 2 years. Bilateral flank pain; 27 lb. weight loss. BSA 1.65 m.^{2}. 170/110. Bilateral costovertebral angle tenderness. BUN: 10 mg.%. Right nephrectomy (June 24, 1963): chronic pyelonephritis with arteriolar necrosis.	Bilateral asymmetry. Right much more involved than left. Intravenous urogram (June 10, 1963): right kidney 13.2 ×4.7 cm.; left kidney 16.2×6 cm.; marked caliectasis and cortical atrophy of right kidney. Renal angiogram (June 17, 1963): decreased caliber of right renal artery; inhomogeneous right nephrogram of decreased intensity with irregular, poorly defined cortical margin and areas of marked cortical atrophy; one area of focal cortical atrophy in the left kidney.
3. D.B., white male, aged 47 years. Hypertension for 18 months. 250/130. Right nephrectomy (April 16, 1962): chronic pyelonephritis (minimal morphologic lesion).	Bilateral asymmetry. Right much more involved than left. Intravenous urogram (April 6, 1962): calcified left renal artery aneurysm; right kidney 10.5×6 cm.; left kidney 16×8.5 cm.; delayed excretion of right lower pole; localized caliectasis in mid-pole of left kidney. Renal angiogram (April 10, 1962): decreased caliber of right artery, aneurysm in inferior subdivision of left renal artery and irregularity (arteriosclerosis) of both renal arteries; bilateral tortuous, poorly filled peripheral arteries; marked atrophy of lower half of right kidney; localized cortical atrophy in mid-pole of left kidney.
4. P.D., white female, aged 7 years. Periorbital edema for 5 weeks. Headaches for 2 weeks. Postprandial vomiting for 2 days. BSA 0.79 m.^{2}. 270/210. Papilledema. Urinalysis: 3+protein; 2–4 granular casts, 1–4 rbc and 12–18 wbc/hpf. BUN: 25 mg.%. Left nephrectomy (Dec. 31, 1963): chronic pyelonephritis (pelvis and calyces dilated; virtually whole cortex scarred).	Bilateral asymmetry. Left much more involved than right. Intravenous urogram (Dec. 20, 1963): right kidney 10 ×4.7 cm.; left kidney 6.4×2.9 cm.; marked decrease in excretion of left kidney; marked bilateral caliectasis with cortical atrophy. Cystogram (Dec. 20, 1963): bilateral ureteral reflux. Renal angiogram (Dec. 21, 1963): decreased caliber of left renal artery; bilateral marked decrease in opacification of intrarenal arteries; marked decrease in intensity of nephrograms (left much more than right).
5. L.B., white female, aged 9 years. Headaches for 3 months. BSA 1.02 m.^{2}. 250/150. Urinalysis: proteinuria; granular casts, fixed	Bilateral asymmetry. Left much more involved than right. Intravenous urogram (May 13, 1963): right kidney 8.3 ×3.8 cm.; left kidney 6.1×3.3 cm.; decreased excre-

Table I—(*Continued*)

Clinical, Laboratory, and Pathologic Data	Roentgenographic Findings
specific gravity (1.003–1.007). BUN: 37 mg.%. Left nephrectomy and right biopsy (June 16, 1963): acute and chronic pyelonephritis; proliferative glomerulonephritis (pyelonephritis probably predominant).	tion on right and no excretion on left. Cystogram (May 13, 1963): trabeculated bladder with left ureteral reflux. Renal angiogram (June 10, 1963): marked decrease in caliber of left renal artery; bilateral tortuous intrarenal arteries with marked peripheral attenuation on left; decreased intensity of nephrograms (left much more than right) with irregular cortical margins.
6. F.G., white male, aged 58 years. Lymphosarcoma for 14 years. Hypertension, intermittent headaches for 7 years. BSA 1.86 m.². 225/115. Bilateral retinal hemorrhages. Urinalysis: occasional granular casts and 0–2 wbc/hpf. BUN: 18 mg.%. Left nephrectomy (Feb. 1, 1961): arteriosclerosis, organizing thrombi (no lesions of radiation nephritis).	Bilateral asymmetry. Left only involved. Intravenous urogram (Jan. 20, 1961): right kidney 15×5.6 cm.; left kidney 7×3.5 cm.; poor excretion and caliectasis of left kidney. Renal angiogram (Jan. 25, 1961): decreased caliber of left renal arteries and decreased opacification of intrarenal ramifications; decreased intensity of left nephrogram with irregular cortical margin.
7. A.P., white female, aged 32 years. Urinary tract infection 12 years ago. Passed 2 urinary tract calculi 11 years ago. Hypertension during pregnancy 9 years ago. Hypertension since toxemia of pregnancy 3 years ago. BSA 1.64 m.². 220/125. Grade II retinopathy. Urinalysis: 3+protein. BUN: 39 mg.%. Left nephrectomy (Oct. 19, 1963): arterial and arteriolar nephrosclerosis (large nonspecific scars).	Bilateral asymmetry. Left much more involved than right. Intravenous urogram (Oct. 4, 1963): right kidney 14.5×6 cm.; left kidney 9×3.3 cm. Renal angiogram (Oct. 14, 1963): marked decrease in caliber and abrupt tapering of left renal artery with marked attenuation and irregularity of intrarenal arteries; decreased intensity of left nephrogram with indistinct cortical margin; slightly irregular and indistinct right cortical margin.
8. F.W., white female, aged 31 years. Panhypopituitarism. Bilateral costovertebral angle pain 1 day. BSA 1.47 m.². 122/78. Left costovertebral angle tenderness. Fever 38.5° C. Urinalysis: 2+protein, 10–12 rbc and 25–30 wbc/hpf. Urine culture: heavy growth of *Proteus*. Hb 8.7 gm. Hct. 29%. Open biopsy, both poles (April 8, 1964): no pathologic diagnosis (nonspecific scar at edge of one section).	Intravenous urogram and retrograde pyelogram (March 31, 1964): right kidney 16.2×7 cm.; left kidney 17×7.5 cm. Renal angiogram (April 3, 1964): bilateral irregular cortical margins.
9. B.D., white female, aged 36 years. Urinary tract infections for 12 years. Labile hypertension (up to 200 mm. Hg systolic) for 5 years. Headaches and pain for 1 month. BSA 1.70 m.². 150/80 (on antihypertensive medication). Urinalysis: 1+protein, many bacteria and 8–10 rbc/hpf. Urine culture: heavy growth of *E. coli*. BUN: 11 mg.%.	Bilateral asymmetry. Left only involved. Intravenous urogram (Feb. 20, 1963): right kidney 11.2×5.3 cm.; left kidney 13×4.1 cm.; caliectasis on left. Renal angiogram (Feb. 20, 1963): slight decrease in caliber and tapering of left renal artery with tortuous attenuated peripheral arteries; localized areas of cortical atrophy with irregular cortical margin.

(*Continued on next page*)

Table I—(*Continued*)

Clinical, Laboratory, and Pathologic Data	Roentgenographic Findings
10. L.G., white female, aged 47 years. Asymptomatic pyuria for 3 years. Right costovertebral angle and flank pain, nausea, vomiting, chills, fever, and gross hematuria for 4 weeks. BSA 1.57 m.^{2}. Blood pressure: normal. Bilateral costovertebral angle tenderness. Urinalysis: 15–20 wbc/hpf. BUN: 14 mg.%.	Bilateral asymmetry. Right more involved than left. Renal angiogram (Dec. 2, 1963): 2 main renal arteries with tapering of cephalad ones on each side; bilateral tortuous, attenuated peripheral arteries; inhomogeneous nephrograms of decreased intensity with cortical atrophy (severe in localized areas) and irregular, indistinct cortical margins; right kidney 10×5 cm.; left kidney 12.5×6.5 cm.
11. A.P., white female, aged 38 years. Left pyelonephritis 17 years ago (infected urine, frequency and left flank pain). Hypertension for 17 years. Sympathectomy for hypertension 16 years ago. Recent inincrease in headaches, dizziness, and fatigue. BSA 1.46 m.^{2}. 174/100. Urinalysis: normal. BUN: normal.	Bilateral asymmetry. Left much more involved than right. Intravenous urogram (Aug. 27, 1962): right kidney 14.5×6.5 cm.; left kidney 7×2.5 cm.; marked cortical atrophy and caliectasis on left. Renal angiogram (Nov. 5, 1962): marked decrease in caliber of left renal artery and attenuation of peripheral ramifications; marked decrease in intensity of left nephrogram with extreme cortical atrophy and irregular, indistinct cortical margin; localized area of cortical atrophy in right kidney.
12. F.B., white female, aged 59 years. Patient told she had "Bright's disease" 15 years ago. Hypertension for 5 years. Episode of urgency, frequency and costovertebral angle tenderness 1 year ago. Fever, chills, and bilateral flank pain 2 months ago which responded to antibiotic therapy. BSA 1.98 m.^{2}. 200/100. Urinalysis: trace of protein, 15 wbc/hpf. BUN: 16 mg.%.	Bilateral asymmetry. Left much more involved than right. Intravenous urogram (July 26, 1961): right kidney 17×6.5 cm.; left kidney 8×3 cm.; poor excretion on left with marked caliectasis; minimal caliectasis of right kidney. Renal angiogram (July 26, 1961): marked decrease in caliber of left renal artery with bilateral marked attenuation of peripheral arteries; marked inhomogeneity and decrease in intensity of left nephrogram with extreme cortical atrophy and irregular, indistinct cortical margin; localized areas of cortical atrophy with irregular cortical margin of right kidney.
Glomerulonephritis	
13. A.B., Negro female, aged 31 years. Hypertension for 10 years. Severe left upper quadrant pain for 48 hours followed by fever of 39°C., hematuria, and oliguria. 160/100. Urinalysis: 4+protein, 2–3 fine granular casts, 60–70 rbc and 5–12 wbc/hpf. BUN: 33–198–18 mg.%. Urine culture: negative. Needle biopsy (June 18, 1962): subacute glomerulonephritis (? lupus erythematosus).	Bilateral symmetry. Intravenous urogram (June 16, 1962): right kidney 15.8×8.5 cm.; left kidney 14×8 cm.; nonexcreting kidneys. Retrograde pyelogram (June 16, 1962): retained contrast material in collecting systems hours after retrograde pyelography; marked attenuation and poor opacification of peripheral arteries with extreme decrease in intensity of nephrograms; persistence of opacification of larger intrarenal arteries; smooth cortical margins.
14. K.M., white male, aged 41 years. Hypertension of unknown duration. BSA 1.97 m.^{2}. 200/120. Urinalysis: 2+protein, 10–20 rbc/hpf. BUN: 16 mg.%.	Bilateral symmetry. Intravenous urogram (Oct. 30, 1963): right kidney 15.1×7.4 cm.; left kidney 13×6.5 cm.; bilateral nephrolithiasis; double right collecting system.

TABLE I—(*Continued*)

Clinical, Laboratory, and Pathologic Data	Roentgenographic Findings
Needle biopsy (Nov. 11, 1963): glomerulonephritis (focal lesions).	Renal angiogram (Oct. 7, 1963): tapering of main renal arteries; marked attenuation and poor opacification of peripheral arteries with extreme decrease in intensity of nephrograms; persistent opacification of larger intrarenal arteries; smooth cortical margins.
15. M.B., white female, aged 35 years. Hematuria for 2 months. Right costovertebral angle pain for 10 days. BSA 1.72 m.^{2}. Blood pressure: normal. Right flank tenderness. Urinalysis: 2+protein, 10–2 rbc/hpf. BUN: 11 mg.%. Needle and open biopsy (March 26, 1964): acute glomerulonephritis.	Bilateral symmetry. Intravenous urogram and retrograde pyelogram (June 3, 1963): right kidney 17×6.5 cm.; left kidney 16.3×7.5 cm. Renal angiogram (March 19, 1964): large kidneys, otherwise normal.
16. R.V.P., white male, aged 42 years. Hypertension and azotemia for 3 years. BSA 2.00 m.^{2}. 160/115. Grade 1 retinopathy. Urinalysis: proteinuria, 8–10 rbc and 4–5 wbc/hpf. Urine culture, negative. BUN: 41 mg.%. PSP: 25% excretion in 4 hours. Creatinine clearance: 37 ml./min. Hb 13.3 gm.	Bilateral symmetry. Intravenous urogram (Jan. 16, 1962): right kidney 12.6×6.5 cm.; left kidney 12×7 cm.; bilateral poor excretion. Retrograde pyelogram: normal. Renal angiogram (Feb. 4, 1963): tapering of main renal arteries; marked attenuation and prolonged opacification of larger intrarenal arteries with no opacification of peripheral branches; extreme decrease in intensity of nephrograms.
Arteriolar Nephrosclerosis	
17. M.T., white male, aged 66 years. Symptoms and signs of basilar artery insufficiency. Hypertension at least 4–5 months. Headaches 4–5 months. Died of carcinoma of the lung. BSA 1.88 m.^{2}. 218/110. Urinalysis: 2–3 wbc and 2–3 rbc/hpf. BUN: 20–42 mg.%. Autopsy (Sept. 20, 1963): arterial and arteriolar nephrosclerosis (many cholesterol occlusions in muscular renal arteries; right kidney 95 gm., left 150 gm.; "vascular scars" grossly).	Bilateral asymmetry. Right slightly more involved than left. Intravenous urogram (Aug. 9, 1963): right kidney 11.5×5.5 cm.; left kidney 13×6 cm.; bilateral irregular cortical margins. Renal angiogram (Aug. 16, 1963): bilateral tortuous, poorly opacified peripheral arteries; inhomogeneous nephrograms with irregular, poorly defined cortical margins.
18. R.S., white male, aged 71 years. "Long standing" hypertension. Several cerebral vascular accidents previously and one immediately prior to admission. Oliguria for 1 day. 220/130. Decerebrate posture. Urinalysis 2+protein, 50 rbc, 1–2 wbc and many red cell casts/hpf. BUN: 74–260 mg.%. Needle biopsy (March 2, 1964) and autopsy (March 14, 1964): arteriolar nephrosclero-	Bilateral symmetry. Renal angiogram (Feb. 29, 1964): left renal artery stenosis with marked decrease in caliber and tapering of left renal artery; attenuation of the large intrarenal arteries on the left with no opacification of the peripheral ramifications, extreme decrease in intensity of left nephrogram; no opacification of right renal artery or kidney.

(*Continued on next page*)

TABLE I—(*Continued*)

Clinical, Laboratory, and Pathologic Data	Roentgenographic Findings
sis (cholesterol occlusion of many muscular arteries).	
19. L.D., Negro female, aged 37 years. Incomplete spontaneous abortion (3 month fetus) 3 weeks ago. Periorbital edema, hypertension and oliguria for 3 days. In coma. 160/100. Retinal hemorrhages and exudates. Urinalysis: 2+protein, many rbc and 3–5 wbc/hpf. Urine culture: heavy growth of *E. coli.* BUN: 119 mg.%. Needle biopsy ×2 (Aug. 13 and 30, 1963) and autopsy (Oct. 18, 1963): arteriolar nephrosclerosis with necrosis and internal hyperplasia (malignant hypertension).	Bilateral symmetry. Intravenous urogram (Aug. 19, 1963): nonexcreting kidneys. Retrograde pyelogram: no urinary tract obstruction. Renal angiogram (Aug. 20, 1963): tapering of main renal arteries; marked attenuation and persistent opacification of larger intrarenal arteries with no opacification of peripheral arteries; absent nephrograms.

ANGIOGRAPHIC FINDINGS

Pyelonephritis (Fig. 1 through 3) occasionally was unilateral, but usually involved both kidneys. When bilateral, the kidneys were not affected equally, and often one kidney was involved much more severely than the other. In 3 of 12 patients (Cases 7, 9, 10), the orifice of the main renal artery was relatively normal in size, but the artery tapered abruptly within its proximal centimeter or two. In all patients the caliber of the main renal artery was decreased in proportion to the extent of parenchymal disease. The major intrarenal arteries were diminished in caliber. The more peripheral arterial ramifications were tortuous or "corkscrew" and in areas of more severe involvement were not seen. The size of the kidney was decreased, often to a marked degree. The intensity of the nephrogram was diminished; the renal cortex was reduced in thickness; and the cortical margin was indistinct and irregular. These arteriographic and nephrographic findings were not uniform in extent, but involved the kidney in an inhomogeneous or "spotty" manner, corresponding to areas of varying degrees of focal parenchymal destruction.

Glomerulonephritis was characterized by bilaterally symmetric involvement of the kidneys. In 1 patient with minimal disease, the kidneys were enlarged, but the angiographic findings otherwise were normal (Case 15). The remaining patients had severe disease, and the angiographic findings were marked (Fig. 4, *A–D*). In 2 patients (Cases 14, 16), the orifice of the main renal artery appeared normal but abruptly tapered to a diminished caliber. The abnormalities involving the intrarenal arteries and nephrogram were uniform in degree throughout each kidney. Opacification of the larger intrarenal arteries was prolonged. These arteries had a "leafless tree" appearance with marked attenuation of the medium-sized vessels and extreme reduction in opacification of the more peripheral ramifications. The diminution in opacification of peripheral arteries was more marked than in pyelonephritis. The renal size was decreased. The nephrogram was homogeneous and markedly reduced in intensity. As a result, the thickness of the renal cortex could not be measured. The cortical margin appeared smooth.

Arteriolar nephrosclerosis was characterized by some angiographic findings which simulated pyelonephritis (Fig. 5, *A* and *B*) and some which resembled glomerulonephritis (Fig. 6, *A* and *B*). Those findings in common with pyelonephritis were tortuosity with poor opacification of the

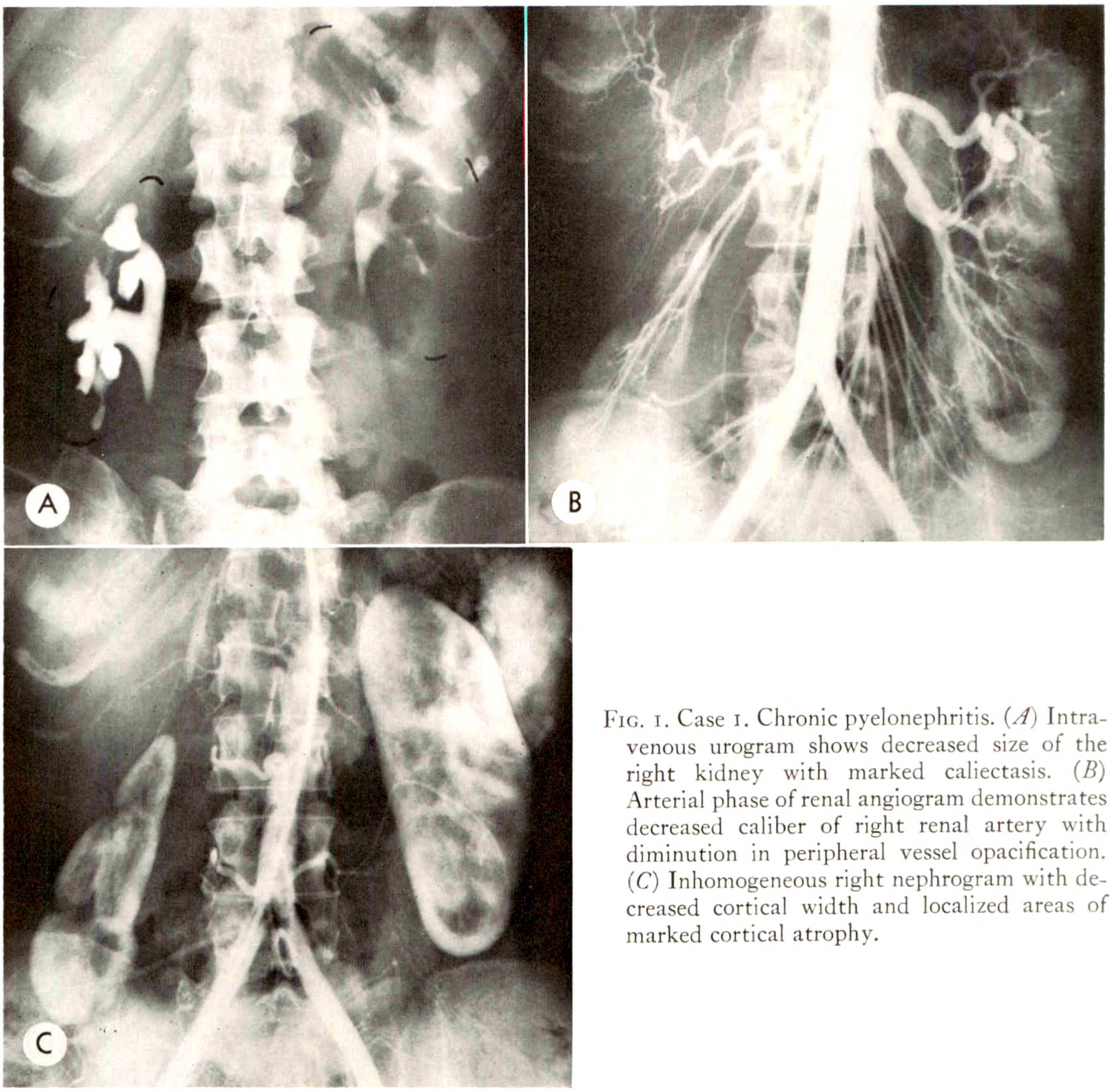

Fig. 1. Case 1. Chronic pyelonephritis. (*A*) Intravenous urogram shows decreased size of the right kidney with marked caliectasis. (*B*) Arterial phase of renal angiogram demonstrates decreased caliber of right renal artery with diminution in peripheral vessel opacification. (*C*) Inhomogeneous right nephrogram with decreased cortical width and localized areas of marked cortical atrophy.

peripheral arteries, inhomogeneity and decreased intensity of the nephrograms, and slight irregularity of the cortical margins. However, nephrosclerosis was characterized by bilaterally symmetric disease and uniform rather than focal involvement of each kidney. The findings which resembled glomerulonephritis included bilaterally symmetric decrease in caliber with prolonged opacification of the larger renal arteries, as well as marked reduction in peripheral vessel opacification and intensity of the nephrogram. However, in nephrosclerosis the nephrogram usually was less homogeneous, and the cortical margin was more irregular. These differential features do not apply to patients with arteriolar nephrosclerosis associated with primary unilateral or bilateral occlusive disease of the main renal arteries. In 2 patients with arteriolar nephrosclerosis the orifice of the main renal arteries was normal, and the vessels tapered markedly in their proximal few centimeters.

PATHOLOGY

The histologic diagnosis of chronic pyelonephritis is difficult. Most of the histologic features accepted in the past are nonspecific and can be found in vascular disease of the

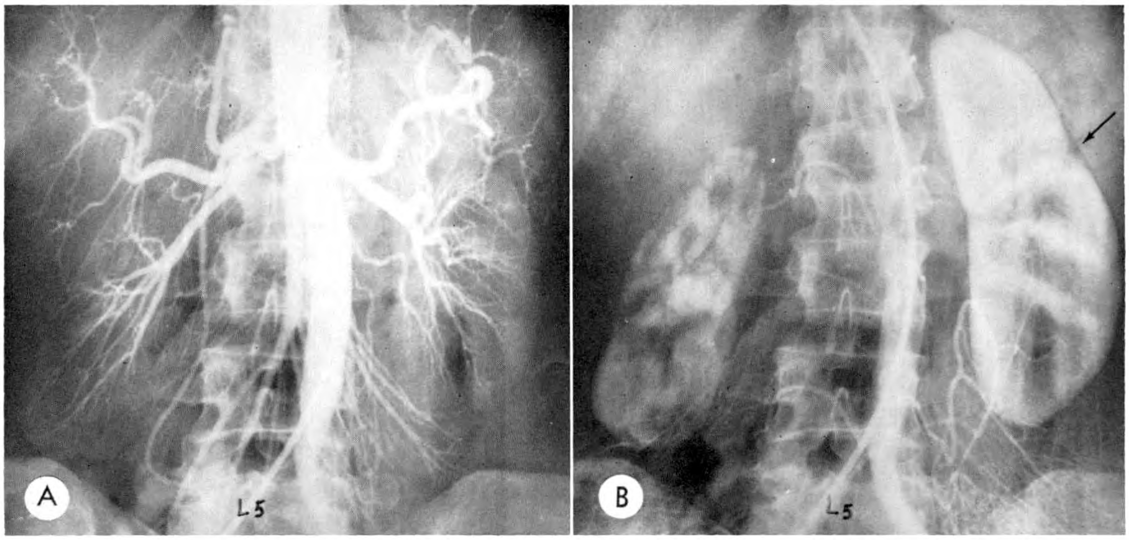

Fig. 2. Case 2. Chronic pyelonephritis. (*A*) Renal angiogram shows decreased caliber of right renal artery. (*B*) Inhomogeneous right nephrogram of decreased intensity with irregular, poorly defined cortical margin and areas of marked cortical atrophy. Arrow indicates focal area of cortical atrophy on the left.

kidneys, as well as pyelonephritis. As emphasized by Kimmelstiel, *et al.*[16] the essential microscopic finding in chronic pyelonephritis is a pleomorphic interstitial inflammatory reaction. Periglomerular fibrosis, thyroid-like areas of tubular dilatation, and a lymphocytic infiltration are not of themselves sufficient for the diagnosis. With such strict pathologic criteria, many renal cortical scars necessarily must be termed simply "non-specific scarring." Clinical and microbiologic findings may suggest that disease of this type actually represents chronic pyelonephritis which has "burned-out" with or without treatment. Cases 7 and 8 are examples of such patients. Pyelonephritis is a disease of the renal interstitium rather than of the functional parenchyma, hence the relative sparing of glomeruli in the scars. It is a *focal disease* which may cause severe renal destruction, yet preserve morphologic re-

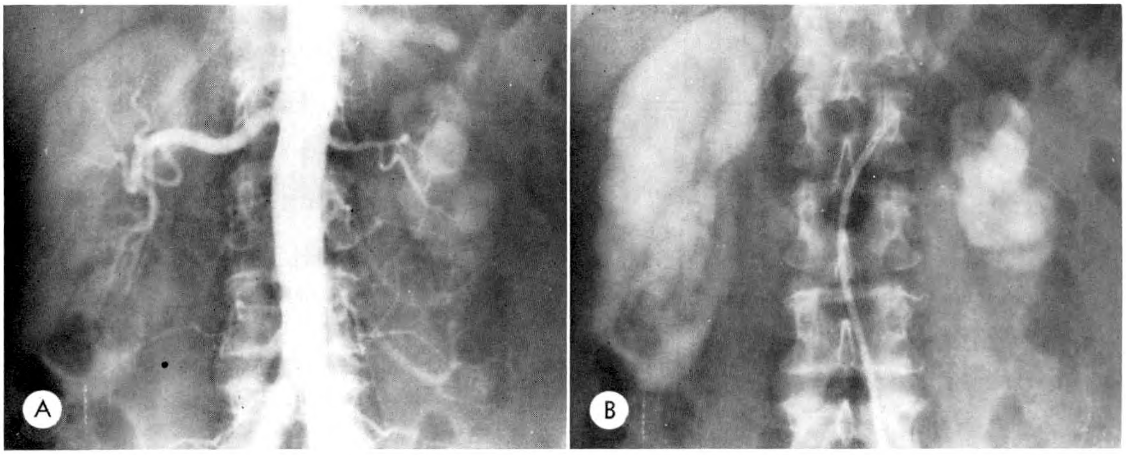

Fig. 3. Case 12. Chronic pyelonephritis. (*A*) Renal angiogram shows marked decrease in caliber of left renal artery with bilateral attenuation of peripheral arteries. (*B*) Marked inhomogeneity and decrease in intensity of left nephrogram with extreme cortical atrophy and irregular, indistinct cortical margin. The right kidney shows localized areas of cortical atrophy and an irregular cortical margin.

flections of its focal character. Asymmetry between the two kidneys is observed more frequently in pyelonephritis than in glomerulonephritis.

Pathologically, glomerulonephritis is a bilateral diffuse renal disease of unknown etiology characterized by glomerular inflammation and its morphologic consequences, exudative, proliferative and later obliterative. An interstitial inflammatory reaction may be present in the acute stage. Tubular atrophy and interstitial fibrosis develop relatively late, presumably from postglomerular ischemia. Traditionally, acute

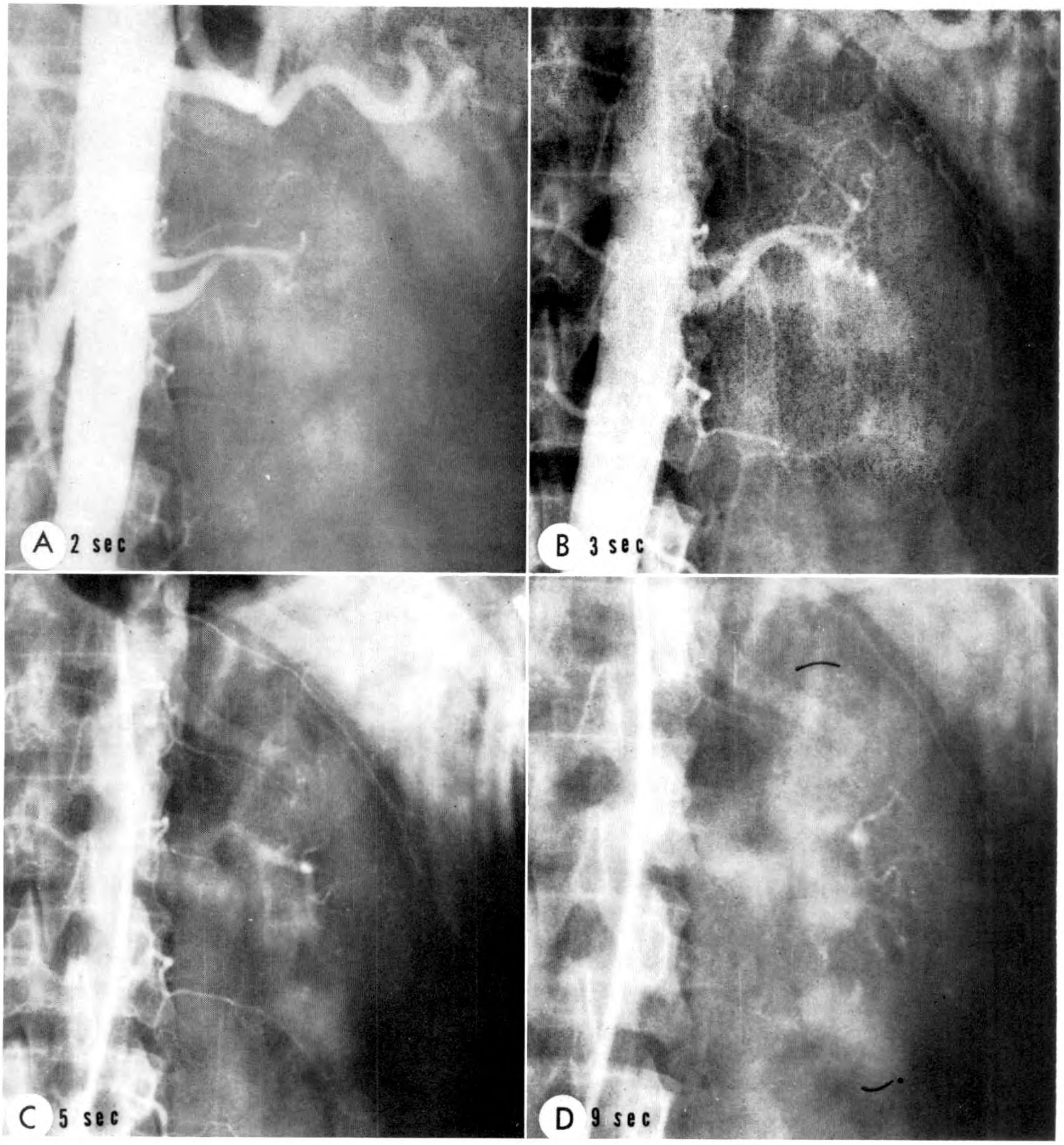

Fig. 4. Case 14. Glomerulonephritis. (*A–D*) Renal angiograms show moderately abrupt tapering of the main renal arteries. This finding also may be demonstrated in patients with pyelonephritis or arteriolar nephrosclerosis. The intrarenal arteries have a "leafless tree" appearance with prolonged opacification of abruptly attenuated larger vessels. The nephrogram is homogeneous but extremely diminished in intensity. The cortical margin is smooth.

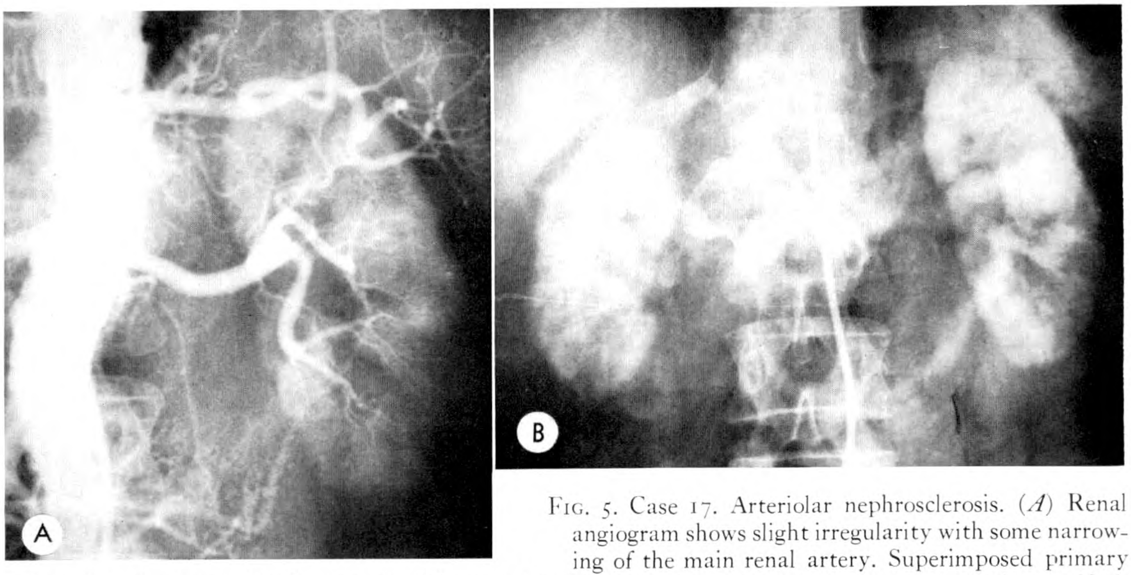

Fig. 5. Case 17. Arteriolar nephrosclerosis. (*A*) Renal angiogram shows slight irregularity with some narrowing of the main renal artery. Superimposed primary branches simulate a distal aneurysm. The peripheral intrarenal arteries are tortuous and poorly opacified. (*B*) The nephrograms are inhomogeneous, and the cortical margins are irregular and not well-defined. Although the angiographic findings superficially may resemble those of pyelonephritis, the bilateral symmetry and the uniform rather than focal involvement of each kidney make nephrosclerosis more likely.

glomerulonephritis is attributed to a renal autoimmunine reaction, usually triggered by previous infection by one of several strains of B-hemolytic streptococci which are referred to as "nephritogenic." With increasing application of percutaneous renal biopsy, two areas of uncertainty have been exposed. The first regards the pathogenesis of glomerulonephritis in patients, often adults, who have no history of antecedent respiratory tract infection and often no serologic evidence of recent streptococcal disease. The second regards the relationship between acute and "chronic sclerosing" glomerulonephritis. Acute glomerulonephritis almost always resolves both clinically and anatomically. "Chronic sclerosing" glomerulonephritis causes death due

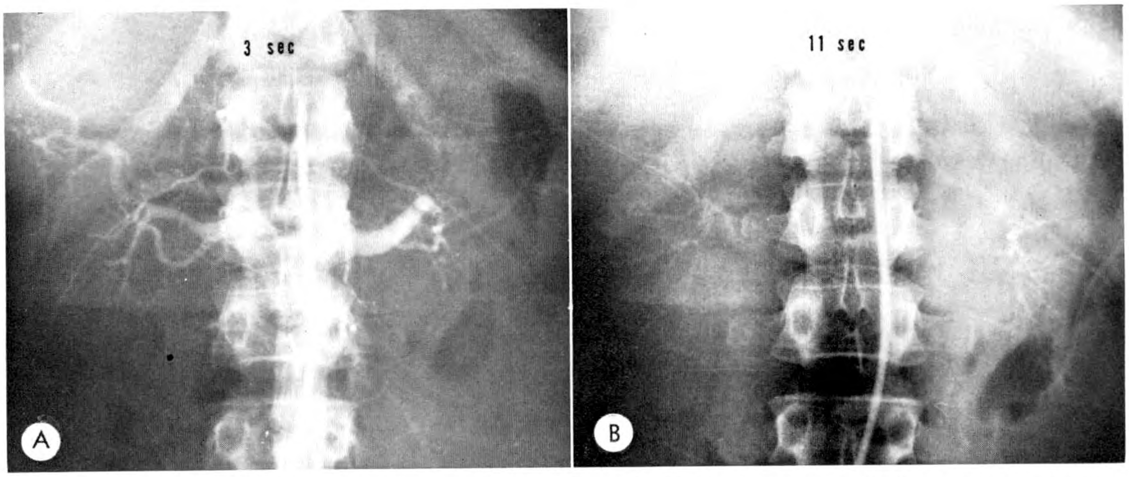

Fig. 6. Case 19. Arteriolar nephrosclerosis. (*A* and *B*) Renal angiograms show marked attenuation and persistent opacification of larger renal arteries; no opacification of peripheral vessels and absent nephrograms. The angiographic findings are indistinguishable from those of severe glomerulonephritis.

to uremia, usually in early or middle adult life. There is some evidence that they may be two distinct and unrelated diseases.[4]

We use the histologic criteria of Jennings and Earle[15] to diagnose acute diffuse glomerulonephritis. These authors emphasize the importance of persistent hypercellularity in the glomerular lobular stalk in making the diagnosis of resolving diffuse glomerulonephritis. The patients in the present series demonstrated the morphologic features of acute or subacute glomerulonephritis. In one patient (Case 13) 2 percutaneous biopsies showed a form of subacute glomerulonephritis in which the focal accentuation of involvement within glomeruli and the conspicuous focal basement membrane thickening strongly suggested lupus erythematosus. This diagnostic distinction is not important in this investigation, because the disease was, nevertheless, a diffuse glomerular inflammation.

Renal vascular disease (nephrosclerosis) is conveniently divided into arteriolar and arterial forms which may coexist but are clinicopathologically distinctive. Arteriolar nephrosclerosis is the morphologic equivalent of essential hypertension. Histologic thickening and eventual hyalinization of renal arterioles apparently is the result rather than the cause of the hypertension, because occasional cases of clinically well-documented hypertension are seen in which the renal arterioles are normal. The clinical syndrome of malignant hypertension is manifested morphologically by *either* necrosis of renal arterioles or by marked subendothelial fibrosis of renal arterioles and small muscular arteries with marked reduction of their lumina. Either form may complicate essential hypertension or chronic renal disease of any type, or may appear *de novo* without predisposing cause.

Arterial nephrosclerosis is associated with scarring of the renal parenchyma consequent to gradually progressing occlusive disease (usually arteriosclerosis) of macroscopic renal arteries. These pathologic findings have few clinical correlates, except in instances where one main renal artery is greatly narrowed (Goldblatt phenomenon). Arterial nephrosclerosis is a disease of the aged. Two cases in this series (Cases 17, 18) are predominantly of this type. These were the oldest patients in the series; both died of extrarenal disease, both had severe aortic atherosclerosis, and both showed numerous occlusions of their intrarenal arteries by organized thrombi which contained (presumably embolic) atheromatous material.

DISCUSSION

Angiography is a well-established method of distinguishing arterial from parenchymal renal disease and unilateral from bilateral involvement. The roentgenographic features which differentiate the unilateral small kidney due to renal artery stenosis, pyelonephritis, and congenital hypoplasia have been outlined.[20] Renal angiography may detect minimal or localized pyelonephritis in patients with little or no evidence of the disease in more routine roentgen studies. The biopsy diagnosis of pyelonephritis is not always reliable, because of the focal nature of renal involvement and because of the difficulty in differentiating pyelonephritis from arteriolar nephrosclerosis. Angiography may assist in distinguishing these 2 diseases and may avoid the hazards of biopsy, especially in patients with critically reduced renal function. Renal angiography may be a useful technique to investigate the natural history and course of chronic renal failure associated with pyelonephritis or arteriolar nephrosclerosis and to evaluate the opposite kidney in patients with unilateral renal artery disease. The technique also may be helpful in determining the cause of graft failure in the postoperative evaluation of transplanted kidneys. Because the clinical and laboratory diagnosis of acute glomerulonephritis is made easily and accurately, the angiographic diagnosis is of less practical importance.

Of major significance in the angiographic differentiation of pyelonephritis,

TABLE II

DIFFERENTIATION OF PYELONEPHRITIS, GLOMERULONEPHRITIS, AND ARTERIOLAR NEPHROSCLEROSIS BY RENAL ANGIOGRAPHY

	Pyelonephritis	Glomerulonephritis	Arteriolar Nephrosclerosis
Basic Characteristics	Bilateral asymmetry with inhomogeneous involvement of each kidney	Bilateral symmetry with uniform involvement of each kidney	Bilateral symmetry with uniform involvement of each kidney
Main Renal Artery	Bilateral asymmetric decrease in caliber corresponding to extent of renal disease	Bilateral symmetric decrease in caliber	Bilateral symmetric decrease in caliber
Intrarenal Arteries	Usually tortuous	Tend to be straight and abruptly attenuated with prolonged opacification	As in pyelonephritis *or* glomerulonephritis
Nephrogram	Intensity moderately diminished, extremely inhomogeneous, cortical margin markedly irregular	Intensity moderately to markedly diminished, homogeneous, cortical margin smooth	Intensity moderately to markedly diminished, moderately inhomogeneous, cortical margin slightly irregular

glomerulonephritis and arteriolar nephrosclerosis (Table II) is the asymmetric involvement of the kidneys in pyelonephritis in contradistinction to the bilaterally symmetric findings in glomerulonephritis of arteriolar nephrosclerosis. Furthermore, pyelonephritis is a focal disease which results in vascular and parenchymal changes of varying degree in the same kidney, whereas glomerulonephritis or arteriolar nephrosclerosis produces changes of uniform intensity throughout each kidney. Decreased caliber or tapering of the main renal artery, as well as reduction in size of the kidney, may be demonstrated in all 3 diseases, and are not helpful in their differential diagnosis.

Meaney *et al.*[18] performed *in vitro* arteriography and pathologic examination on kidneys removed from normal and hypertensive patients. In the 12 normal patients the large, medium-sized, and peripheral intrarenal arteries tapered gradually and uniformly from the main renal artery distally. The cortical arterioles were well-filled, uniformly distributed, and extended almost to the periphery of the renal parenchyma. *In vivo* angiography also demonstrates these findings in the normal kidney (Fig. 7).

Of the 16 hypertensive patients reported by Meaney *et al.*, 8 had arteriolar nephrosclerosis, 4 had glomerulonephritis, and only 1 had infectious disease. The patients with advanced vascular disease associated with the hypertension showed a decrease in caliber and irregularity of the medium-sized renal arteries. Heptinstall *et al.*[18] showed that pyelonephritis induced experimentally in rabbits produced tortuosity of medium-sized intrarenal arteries. Our patients with pyelonephritis, glomerulonephritis, or arteriolar nephrosclerosis showed a decrease in caliber and tortuosity of the medium-sized renal arteries. However, severe glomerulonephritis appeared to be associated with more abrupt attenuation and less tortuosity of these vessels.

All kidneys from hypertensive patients reported by Meaney *et al.* showed decreased or absent filling of the cortical arterioles. These authors concluded that the absence of cortical arteriolar filling indicated a reduction in luminal size of these vessels and, by inference, the presence of cortical ischemia. Peripheral arteriolar opacification was reduced in our patients with pyelonephritis, glomerulonephritis, or arteriolar nephrosclerosis and was not a reliable feature in their differential diagnosis, although these changes were more pronounced in severe glomerulonephritis or arteriolar nephrosclerosis. In the chronic pyelonephritic kidneys, associated vascular obstruction probably contributed to this effect.[17]

The nephrogram phase of the renal angiogram is the most useful in differentiating pyelonephritis, glomerulonephritis, and arteriolar nephrosclerosis. Homogeneity of the nephrogram and smoothness of the cortical margin are greatest in glomerulonephritis, less in arteriolar nephrosclerosis, and least in pyelonephritis. Intensity of the nephrogram is a less distinctive feature, although it tended to be more diminished in patients with glomerulonephritis and arteriolar nephrosclerosis. Shaldon *et al.*[25] recently have suggested that the absent nephrogram during renal arteriography in patients with acute renal failure is due to a selective redistribution of blood flow in the oliguric kidney with reduction in flow to the cortex. Most of our patients were hypertensive, and the decrease in peripheral arteriolar opacification and intensity of the nephrogram in these patients probably was associated with cortical ischemia responsible for the hypertension, as suggested by Meaney *et al.*

Boijsen[2] has described temporary peripheral vasoconstriction and ischemia with an irregular cortical margin during angionephrography of the normal kidney. We do not believe we have encountered this phenomenon which may simulate the changes of pyelonephritis. Bilateral "end stage" kidneys due to severe pyelonephritis may appear fairly symmetric. We have not investigated patients in this category and, therefore, are not certain that these kidneys can be distinguished angiographically from the "end stage" kidneys in patients with severe glomerulonephritis or arteriolar nephrosclerosis. Although this distinction is of considerable theoretic interest, it is of questionable practical value at present. The renal angiography findings in the 3 patients with histologically proven arteriolar nephrosclerosis were difficult to distinguish from those in severe glomerulonephritis. Greenspan, Ricketts, and Simon[9] have reported *in vivo* magnification angiography of the kidneys, using a roentgenographic tube with an effective focal spot of 0.26 mm. This technologic development makes possible more detailed angiographic examinations and may provide a more precise method of distinguishing pyelonephritis from glomerulonephritis and of evaluating nephrosclerosis and other forms of renal disease.

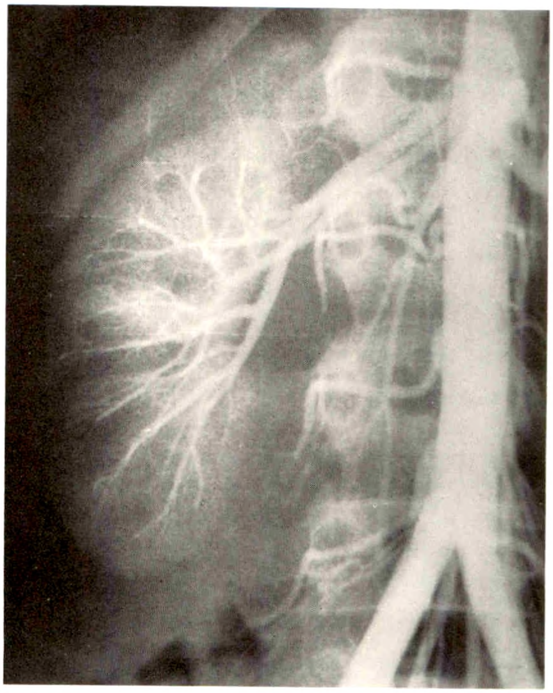

FIG. 7. Normal renal angiogram in a 12 year old girl. The large, medium-sized, and peripheral arteries are uniform in caliber and taper gradually. The early nephrogram is homogeneous; the cortex is normal in width and smooth in contour.

SUMMARY AND CONCLUSIONS

The vascular patterns and nephrograms during renal angiography in patients with chronic pyelonephritis, glomerulonephritis, and arteriolar nephrosclerosis are described.

In chronic pyelonephritis both kidneys usually are affected, but the severity of involvement is not bilaterally symmetric. The main renal arteries are decreased in caliber asymmetrically, according to the severity of renal disease. The intrarenal arteries are tortuous or "corkscrew;" the nephrogram is diminished in intensity and extremely inhomogeneous; the cortex is reduced in thickness; and the cortical margin is indistinct and markedly irregular. These angiographic and nephrographic findings are not uniform in extent, but involve the kidney in an inhomogeneous or "spotty" manner, corresponding to areas of varying degrees of focal parenchymal destruction.

Glomerulonephritis and arteriolar nephrosclerosis are characterized by bilaterally symmetric involvement of the kidneys and uniform changes throughout each kidney. The main renal arteries are decreased in caliber symmetrically. In glomerulonephritis the intrarenal arteries may have a "leafless tree" appearance with prolonged opacification of abruptly attenuated larger vessels. Opacification of the more peripheral ramifications may be reduced markedly. The nephrogram is homogeneous and often is extremely reduced in intensity. The cortical margin is smooth.

In moderate arteriolar nephrosclerosis the intrarenal arteries may be tortuous or "corkscrew," but with severe disease they may simulate those in glomerulonephritis. The nephrogram is moderately inhomogeneous and reduced in intensity, and the cortical margin is slightly indistinct and irregular.

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RENAL ARTERIOVENOUS FISTULAE*

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JOHN Hunter first described arteriovenous fistulae over 200 years ago. Reid, in 1902, was the first to observe that organic cardiac disease was frequently associated with these vascular lesions. Since then arteriovenous fistulae have been found in a variety of other anatomic locations, including the kidney.

CLASSIFICATION

Intrarenal arteriovenous fistulae may be classified as (A) congenital due to arteriovenous malformations or (B) acquired.[8,20] In the acquired group are: (1) fistulae following rupture of an arterial aneurysm;[3] (2) traumatic arteriovenous fistulae resulting from penetrating trauma,[14,17] trauma of renal tissue in association with nephrolithotomy,[3,21] partial nephrectomy[20] or percutaneous needle biopsy of the kidney;[3] (3) arteriovenous fistulae in renal carcinoma, where the tumor has eroded the vein;[2,5,10,11,15,16,19] and (4) stump fistulae following nephrectomy.[6,8,20]

As of October, 1964,[13] 55 cases of this condition had been reported. Thirty-five cases have been associated with functioning kidney and on an etiologic basis were divided as follows: congenital, 5 and acquired, 30. The latter group included 6 cases of hypernephroma, 11 of trauma, 3 of inflammation, 1 of arteriosclerosis and 1 idiopathic.

We have recently had the opportunity of studying 5 cases of intrarenal arteriovenous fistulae: 1 congenital, 2 traumatic, 1 neoplastic and 1 following rupture of an arterial aneurysm.

REPORT OF CASES

Case I. H.H., an 18 year old Negro female, was admitted to Cook County Hospital on February 23, 1964, 2 hours after receiving a large penetrating stab wound into the right flank. The patient had no history of surgery, renal disease, heart disease or hypertension.

On physical examination the blood pressure was 110/60 mm. Hg, pulse 120 per minute, respiratory rate 24 per minute, and temperature 100° F. The remainder of the physical examination was negative except for a slightly tender mass in the right flank region and a distended bladder. A catheter was inserted into the bladder and 450 cc. of grossly bloody urine, containing fresh clots, was removed. The urine remained grossly bloody. The right flank mass did not increase in size but there was a progressive decrease in right flank tenderness. An intravenous pyelogram was done (Fig. 1). The hematuria cleared after 1 week. Fifteen days after admission, retrograde femoral arteriograms were obtained (Fig. 2, *A* and *B*) and demonstrated an intrarenal arteriovenous fistula in the lower pole of the right kidney. At this time, a questionable bruit was noted in the right flank area.

At surgery, the right perirenal space was filled with organizing hematoma and a thrill was palpated over the hilar region near the middle and lower pole. A right nephrectomy was performed. Microscopic sections revealed fistula formation in the perihilar region at the junction of the middle and lower thirds of the right kidney.

Case II. C.B., a 38 year old Negro female, was admitted to Cook County Hospital on March 10, 1964, complaining of persistent occipital headaches. The patient had had several previous admissions for episodes of congestive heart failure and was a known hypertensive, having been treated with various antihypertensive drugs, diuretics and digitalis. There was no history of trauma, renal disease, hematuria or flank pain.

The blood pressure was 210/140 mm. Hg, pulse 90 per minute and respiratory rate 18 per minute. The remainder of the physical examina-

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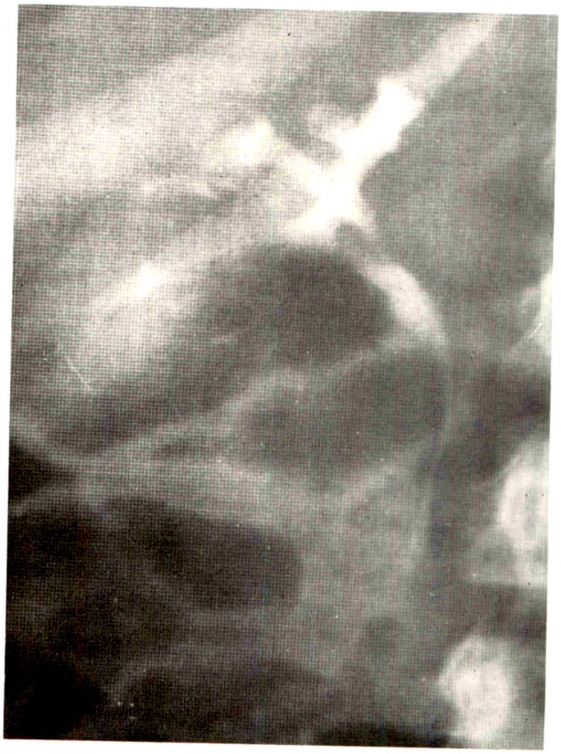

Fig. 1. Case i. Intravenous pyelogram made immediately prior to arteriography. Large poorly defined renal shadow with compression of the pelvis and lower calyces is noted and there is probable extravasation from the lower pole calyx.

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tion was negative except for the finding of Grade 2 hypertensive retinopathy. Urinalysis was negative, and a chest roentgenogram showed slight cardiac enlargement of the aortic or hypertensive configuration. An intravenous pyelogram was interpreted as being within normal limits (Fig. 3). Retrograde femoral arteriograms were done (Fig. 4, *A* and *B*) and demonstrated an intrarenal arteriovenous fistula in the lower pole of the right kidney.

At surgery, a thrill was palpated over the perihilar region of the middle and lower thirds of the right kidney. A total right nephrectomy was performed. No significant change in blood pressure had been noted postoperatively.

Case iii. E.L., a 27 year old white male, had fallen from a height of approximately 25 feet, landing on a cement abutment, and injuring the right side of his abdomen and flank on December 13, 1964, immediately following which he was admitted to the hospital.

Physical examination revealed crepitation over the right posterior aspect of the thorax, blood pressure of 135/70 mm. Hg, respiratory rate of 18 per minute and pulse rate of 90 per minute. The abdomen was scaphoid and firm with guarding and rebound, particularly in the right upper quadrant; bowel sounds were ab-

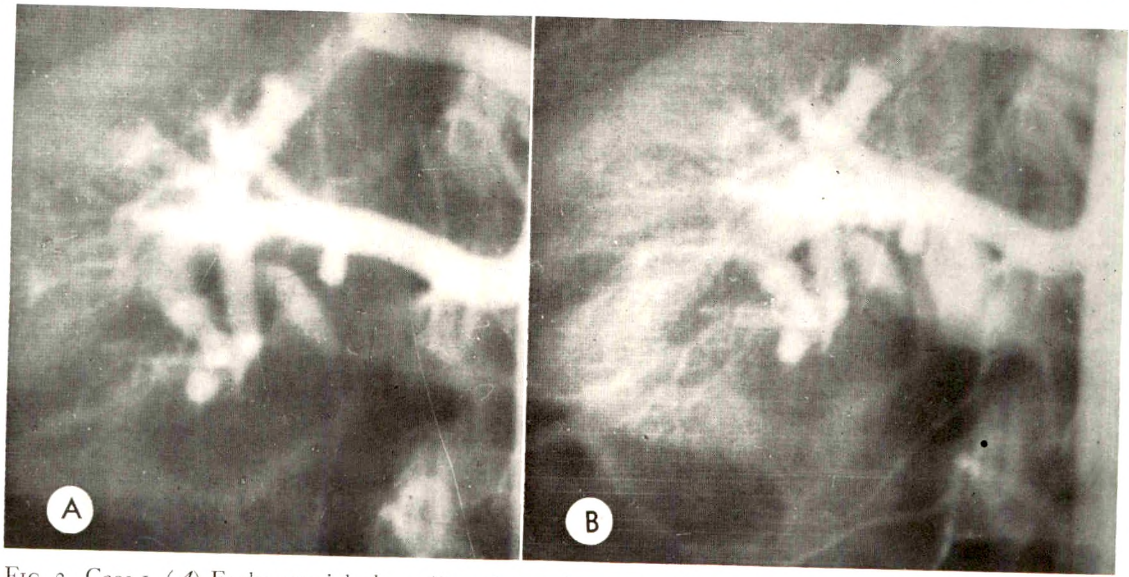

Fig. 2. Case i. (*A*) Early arterial phase ($\frac{1}{2}$ sec.) reveals arterial filling with extravasation of material into pools at lower pole. (*B*) (1 sec.) Note the faintly visualized inferior vena cava and the renal vein overlying the main renal artery.

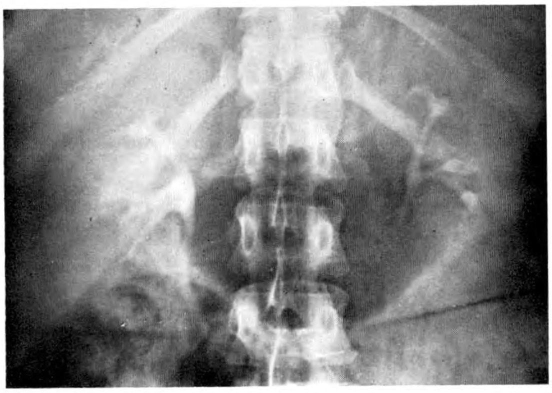

FIG. 3. Case II. Normal intravenous pyelogram.

sent. The patient was passing grossly bloody urine and had a hematocrit of 42 per cent. A chest roentgenogram demonstrated several rib fractures on the right side. Intravenous pyelography revealed nonfunction on the right at 1, 5, and 10 minutes. A cystogram was reported as normal. Paracentesis was negative.

Surgery revealed a retroperitoneal hematoma on the right which was removed, 4 days after admission. The patient made an uneventful recovery and was discharged from the hospital.

A repeat intravenous pyelogram after discharge from the hospital revealed function of both kidneys with extravasation from the superior calyx of the right kidney (Fig. 5). Renal angiograms (Fig. 6; and 7, *A* and *B*) were done 12 days after surgery and were interpreted as demonstrating an intrarenal arteriovenous fistula in the superior pole of the right kidney. Physical examination was essentially negative except for severe pain in the right flank. A right nephrectomy was performed on October 3, 1964 (20 days after accident), revealing a transverse fracture of the upper pole through the hilus and a longitudinal fracture through the posterior aspect of the right kidney.

CASE IV. This patient, a 62 year old Mexican male, entered Cook County Hospital on December 6, 1963, with chief complaints of hematuria, dysuria, and bladder pain of 2 days' duration. Due to acute urinary retention, the bladder was catheterized and 1,200 cc. of grossly bloody urine was withdrawn. Patient denied previous surgery, high blood pressure or urinary complaints.

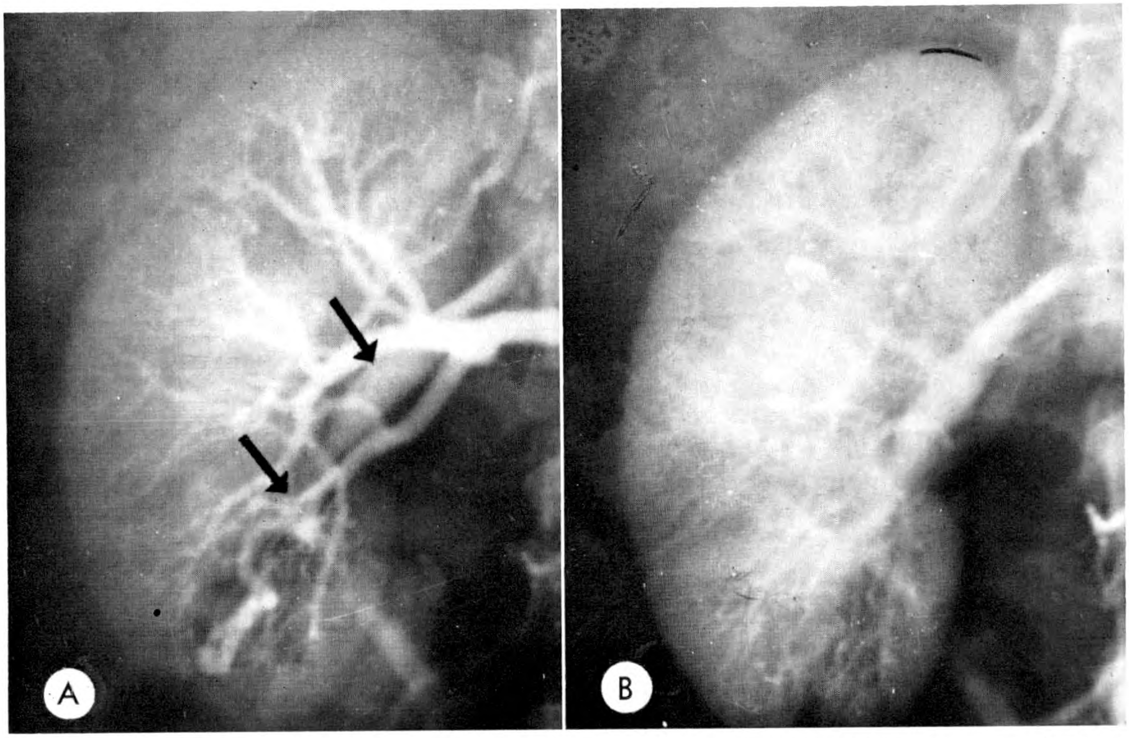

FIG. 4. Case II. (*A*) ($1\frac{1}{2}$ sec.) Arcuate-appearing arteriovenous communication at lower pole. Arrows indicate premature filling of the renal vein. (*B*) (2 sec.) Arterial visualization still noted. Renal vein faintly opacifying the inferior vena cava.

On physical examination the patient had a blood pressure of 140/80, pulse of 72 per minute, respiratory rate of 16 per minute and a Grade 3/6 murmur of aortic stenosis. Laboratory studies revealed a hematocrit of 35 per cent, a blood urea nitrogen of 21 mg. per cent and a hemoglobin of 10.6 gm. per cent. An intravenous pyelogram was interpreted as showing a normal upper collecting system on the left and slight function on the right, insufficient for diagnosis. A right retrograde pyelogram (Fig. 8) demonstrated an irregular filling defect in the superior pole of the right kidney with compression of the calyces. A retrograde femoral arteriogram demonstrated a tumor of the right kidney with arteriovenous fistulae and early filling of the inferior vena cava (Fig. 9; and 10).

At the time of surgery, a loud thrill was palpated over the hilus of the kidney. Three distinct tumor masses were noted in the upper pole of the resected kidney. Diagnosis: adenocarcinoma (clear cell).

Case v. F.M., a 51 year old Negro female, presented with a chief complaint of chest pain. The patient had been at another clinic where she had been treated for hypertension since 1959. Two previous surgical procedures had been done: a colostomy for a rectal stricture secondary to lymphogranuloma venereum and a total hysterectomy for fibroids. No renal biopsy had ever been done, and no significant history of trauma was obtained. Physical examination revealed a blood pressure of 200/120 and a pulse of 80 per minute. Funduscopy revealed Grade 2 hypertensive retinopathy. A continuous bruit was heard over the right flank posteriorly.

Laboratory data were as follows: circulation time 11 seconds, blood urea nitrogen 14 mg. per cent, hemoglobin 72 per cent, red blood cell count 4,120,000, white blood cell count 5,800, and a normal electrocardiogram.

Split function studies revealed equal values and equal concentration of indigo carmine dye bilaterally. There was, however, 2–3x creati-

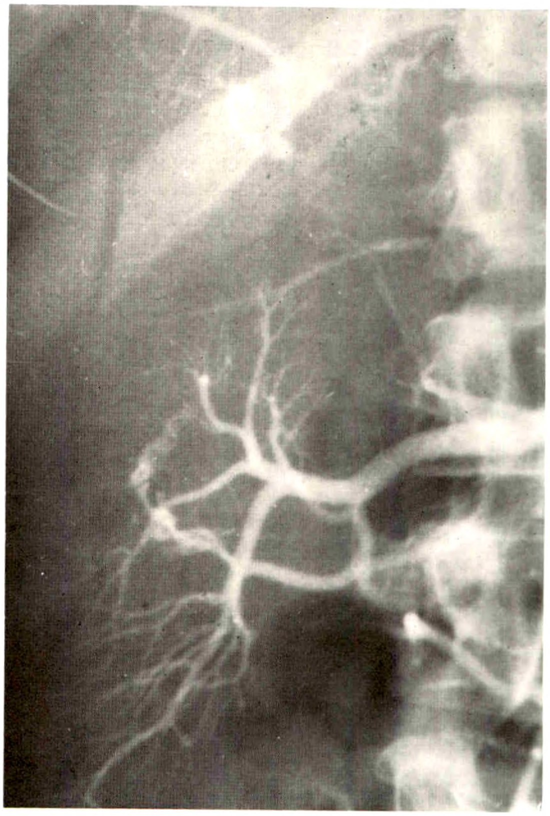

Fig. 6. Case iii. ($\frac{1}{4}$ sec.) Arcuate arteriovenous communication in the upper pole. Note fracture of the 12th rib.

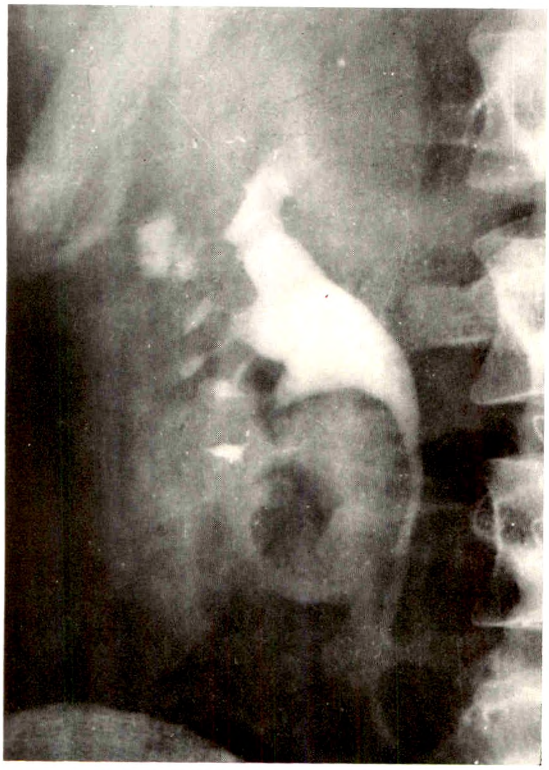

Fig. 5. Case iii. Intravenous pyelogram showing enlarged renal outline with compression of the superior calyces and extravasation of contrast material outside the superior calyx.

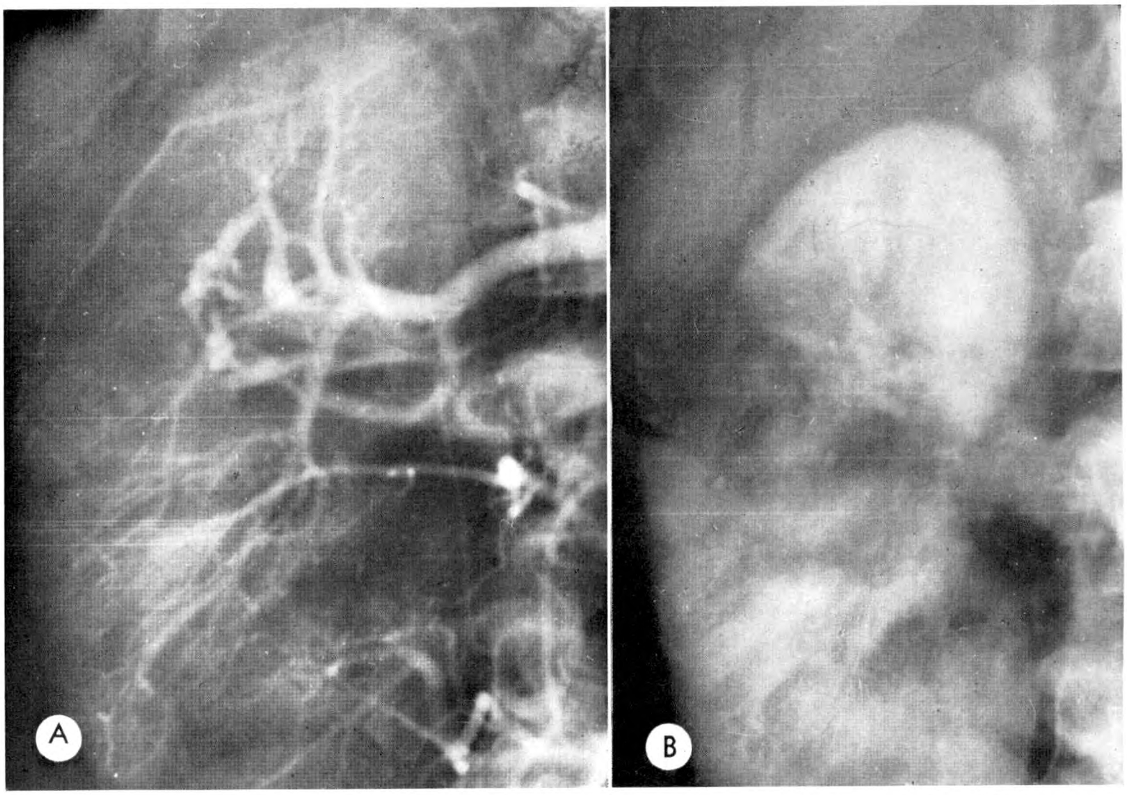

FIG. 7. Case III. (*A*) ($\frac{3}{4}$ sec.) Note faint opacification of the renal vein just below the dorsal branch renal artery. (*B*) ($3\frac{1}{2}$ sec.) Complete laceration noted in the upper pole on nephrogram.

nine concentration on the right as compared to the left.

An intravenous pyelogram (Fig. 11) revealed a compression defect in the lower pole of the right kidney. Renal arteriograms (Fig. 12; and 13) demonstrated an arteriovenous fistula at the site of the ruptured aneurysm.

The patient refused any further treatment.

ROENTGENOGRAPHIC FINDINGS

Many diagnostic procedures are now available for the demonstration of renal arteriovenous fistulae which formerly were diagnosed only by auscultation or surgical exploration. It is not possible to demonstrate any characteristic of arteriovenous

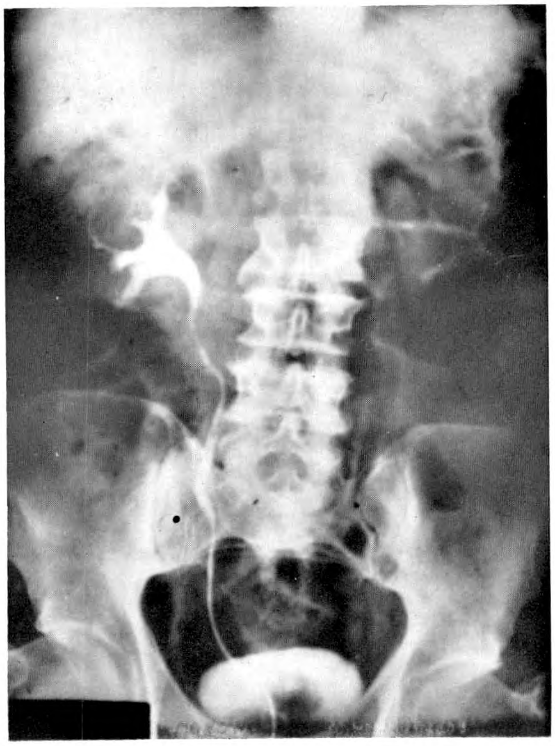

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FIG. 8. Case IV. Right retrograde pyelogram showing a mass compressing the upper pole of the right kidney with flattening of the middle calyx.

fistulae by urography except semicircular calcification[4,12,18] seen at the site of an aneurysm, which occasionally ruptures to produce arteriovenous fistulae. There may be nonvisualization on urography, or there may be irregular filling of the renal pelvis and calyces due to coagulum or fistula (in the latter case the possibility of the presence of tumor must be considered.)[3] The 2 cases (Case I and III) resulting from trauma presented compression defects and extravasation outside of the calyces. The cases of tumor and ruptured aneurysm (Case IV and V) showed compression defects of calyces with no evidence of calcification. The intravenous pyelogram of the congenital case (Case II) of arteriovenous fistula was considered to be within normal limits.

The more widespread use of renal angiography may be credited with the marked increase in the number of cases diagnosed during the past decade. The prompt visualization of the renal vein and inferior vena cava following arterial injection of contrast material,[3,16,22] associated with an increase in size of the renal vein, strongly suggests the presence of a renal arteriovenous fistula.[22] The angiographic findings of increased, serpentine arteries with direct communication of the renal vein, of course, offer an unequivocal diagnosis.[9] The amount of shunting will determine the degree of opacification of the inferior vena cava.

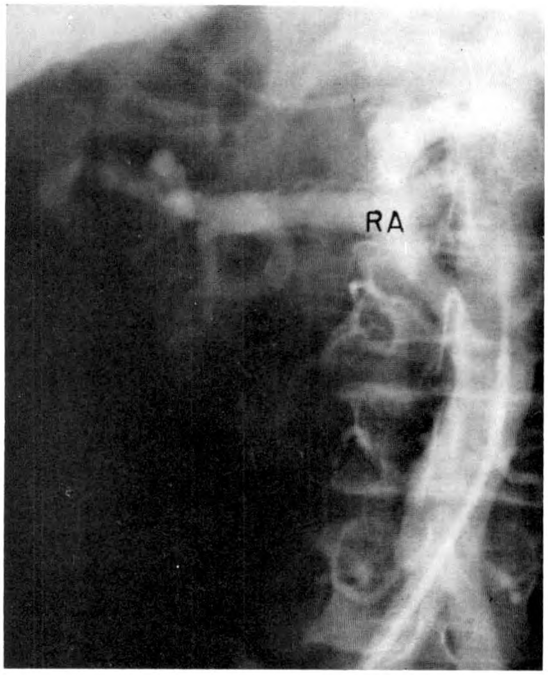

Fig. 9. Case IV. ($\frac{1}{2}$ sec.) Enlarged right renal artery (RA). No tumor vessels are identified.

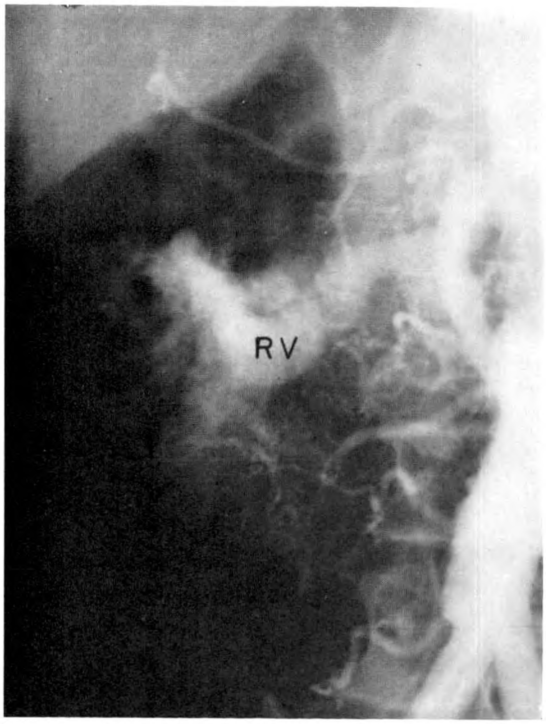

Fig. 10. Case IV. (1 sec.) Rapid appearance of an enlarged renal vein (RV) with minimal tumor stain around it. Faintly visualized inferior vena cava.

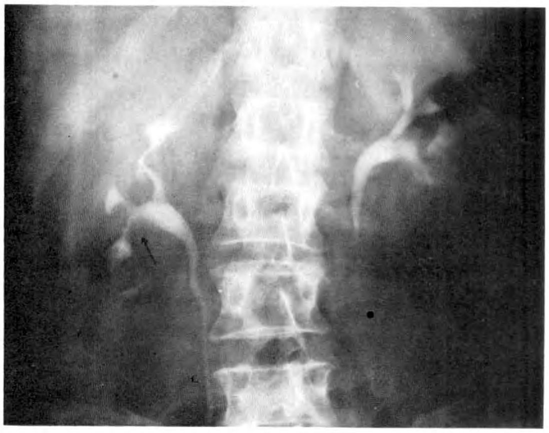

Fig. 11. Case V. Intravenous pyelogram showing mild clubbing and some degree of compression of the lower pole calyces (arrow).

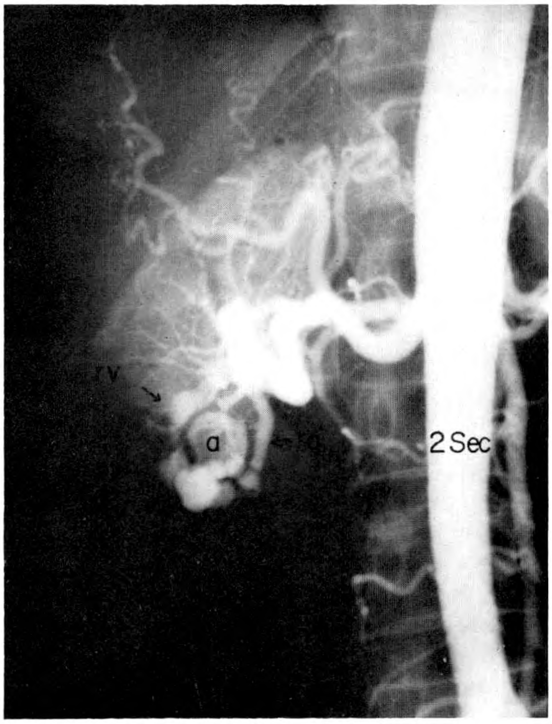

Fig. 12. Case v. (2 sec.) Arteriogram shows a large right renal artery which has a large lower pole branch which erupts into an aneurysm (a). Beginning premature opacification of a renal vein branch slightly lateral to the aneurysm is noted.

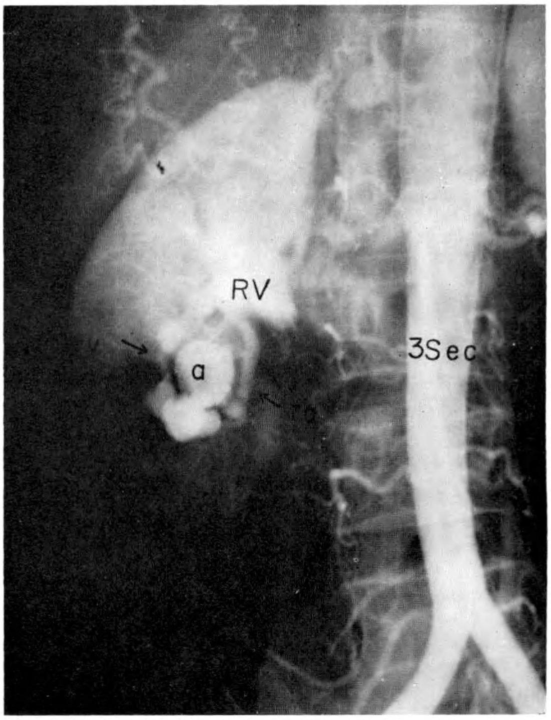

Fig. 13. Case v. (3 sec.) Arteriogram shows well visualized aneurysm (a). The clear space around it represents a clot. The large main renal vein (RV) is now filled and there is continued visualization of the renal artery branch.

DISCUSSION

Renal arteriovenous fistulae may be accompanied by any of the following findings: increase in cardiac output and blood volume; decrease in circulation time; and an increase in oxygen saturation of blood in the renal veins[7,19] (venous oxygen saturation levels are a diagnostic aid not widely used because of the difficulty in obtaining accurate determination). The single most important physical finding is a palpable thrill and a continuous audible bruit over the upper abdomen and flank.[1] Complications are cardiac failure[6,19,22] as a result of hypertension and greatly dilated veins, together with the resulting conditions (thrombophlebitis, ulceration and gross hemorrhage).[6]

SUMMARY

Five cases of renal arteriovenous fistulae, diagnosed by renal angiography, are presented. The diagnostic criterion is premature filling of the renal vein and inferior vena cava. Two cases resulted from trauma, one was congenital, one was due to hypernephroma, and the last case resulted from rupture of an aneurysm into a renal vein branch.

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INTRARENAL ARTERIOVENOUS FISTULA AND ANEURYSM*

A COMPLICATION OF PERCUTANEOUS RENAL BIOPSY

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DURING the past 2 years, 9 cases of intrarenal arteriovenous fistulae and 2 aneurysms have been encountered. These were demonstrated by arteriography on patients who had prior percutaneous renal biopsy and who were being evaluated for hypertension. Healing has been demonstrated by repeat arteriograms in several cases. Neither arteriovenous fistula nor aneurysm produced apparent alteration in the clinical course or evolution of the hypertensive process.

Percutaneous renal biopsy is an important diagnostic procedure in the evaluation of renal disease[5,8,12] and hypertension.[23,24] The frequency of occurrence and ultimate fate of vascular alteration secondary to biopsy have not been discussed previously.

METHODS AND MATERIALS

From July, 1962 through May, 1964, 210 renal arteriograms were made on 188 hypertensive patients as part of a kidney hypertensive study conducted in our institution (Table I).

The transfemoral percutaneous Seldinger[20] method was used with radiopaque catheters, image intensifier control, and with filming by a Sanchez-Perez serialograph.

Percutaneous renal biopsy was performed on 148 of the 188 patients in the study. The Franklin modification of the Vim-Silverman needle was used with the patient in the sitting position. In certain instances, biopsy was performed under image intensifier control in the decubitus position.

RESULTS

A review of the series revealed 58 patients who had percutaneous renal biopsy prior to renal arteriography and 90 patients who had biopsy following arteriography (Table I). The order of procedure was determined by scheduling convenience without predetermined selection. Eleven patients had arteriographic evidence of arteriovenous fistula or aneurysm (Table II). These were found in the group having biopsy prior to arteriography. Of the 90 patients who had biopsy following arteriography, there was only 1 patient who had an aneurysm; however, this aneurysm was of the main renal artery and there were concomitant aneurysms of the splenic and hepatic arteries.

TABLE I

Patients who had renal arteriograms	188
No. of arteriograms performed	210
Patients who had percutaneous renal biopsy	148
Biopsy preceding arteriography	58
Biopsy following arteriography	90

The 11 patients having intrarenal vascular abnormalities were followed clinically and 7 of these patients had repeat arteriographies. The arteriovenous fistula disappeared in 3 cases, became smaller in 1 case and persisted in 2 cases. One aneurysm became smaller.

ILLUSTRATIVE CASES

CASE 1. G.H., a 59 year old female with known hypertension for 20 years, was admitted

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Table II

Case	Age	Sex	Hospital No.	X-Ray No.	Date of Biopsy	Biopsy Side	Date of Arteriography	Results	Comments
G. H. (Case 1)	59	F	133328	162531	12-5-63 12-9-63	Right Left	12-13-63 3-24-64	Left AVF Normal	Healing in 3½ mo.
M. S. (Case 2)	62	F	127579	140149	11-15-62 11-21-62	Right Left	11-23-62 7-24-64	Right AVF Normal	Disappearance by 20 mo.
M. W. (Case 3)	63	F	106856	142396	4-22-63 4-26-63	Right Left	4-30-63 8-12-64	Left AVF Left AVF smaller	Partial healing
H. J. (Case 4)	39	M	98305	153374	3-16-63 3-22-63 8-28-63	Right Left Both	3-25-63 2-6-64	Left AVF Left AVF	Persistence over 11 mo. period
B. B. (Case 5)	57	F	77889	137225	3-2-64 3-9-64	Right Left	6-14-63 3-4-64 7-24-64	Normal Right AVF Right AVF	Normal before biopsy; AVF after biopsy; persistent at 16 mo.
J. C. (Case 6)	36	F	5571	105979	3-17-64	Right	3-13-64 5-9-64	Normal Left AN	Normal before biopsy; development of aneurysm within 8wk.
R. R.	48	F	66496	139598	2-20-64	Left	2-24-64 10-5-64	Left AVF Normal	Disappearance by 7½ mo.
G. M.	40	F	136410	118391	2-18-63	Right	2-26-63	Right AVF	
J. L.	31	M	94666	152708	5-23-62 2-23-63	Right Left	3-1-63	Right AVF	
J. R.	32	M	140379	157730	6-22-63	Right	7-23-63	Right AVF	
O. K.	40	F	18184	117110	4-23-63 5-2-63	Right Left	5-7-63 11-17-64	Left AN Left AN smaller	Smaller at 18 mo.

AVF = Arteriovenous fistula; AN = aneurysm.

for hypertensive work-up in December, 1963. Right renal biopsy was performed on December 5, 1963 without difficulty. Left renal biopsy was performed on December 9, 1963.

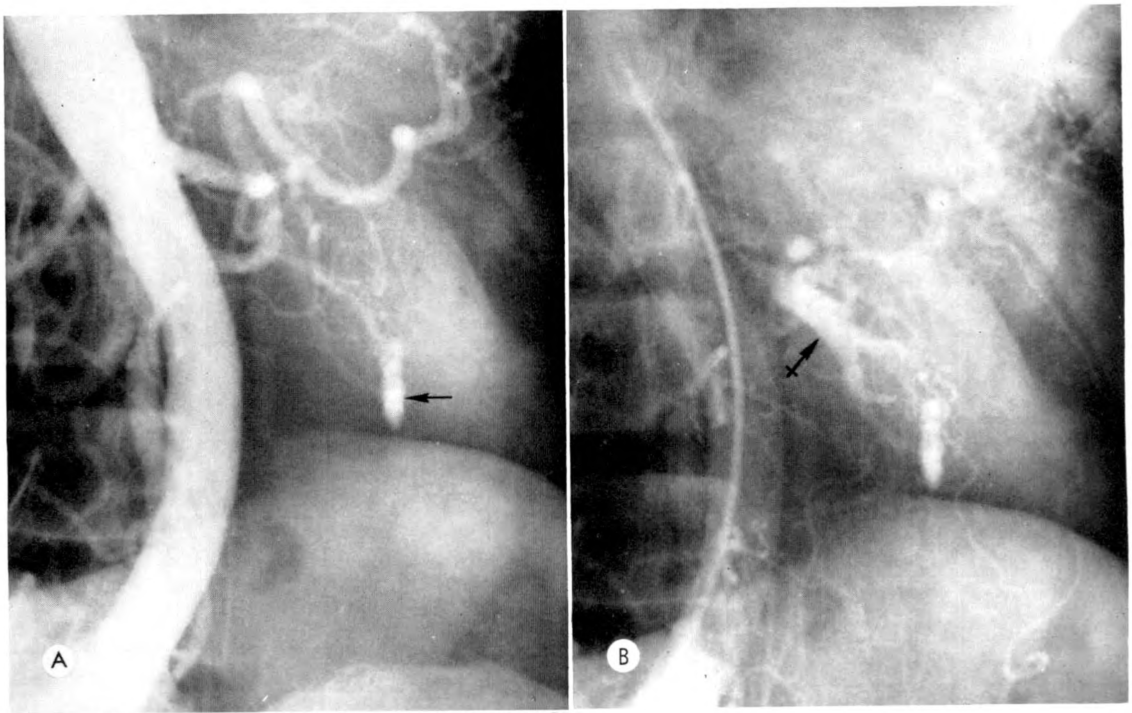
The renal arteriogram on December 13, 1963 showed narrowing of the left renal artery at its take-off with post-stenotic dilatation (Fig. 1*A*). In the left lower pole, there was irregular pooling of contrast material with visualization of a venous drainage trunk indicative of an arteriovenous fistula. The lower pole of the kidney showed enlargement suggesting an intra- or peri-renal hematoma (Fig. 1*B*).

The patient was re-admitted in March, 1964 for repeat studies. The renal arteriogram revealed no evidence of the arteriovenous fistula seen 3 months previously. The lower pole contour appeared within normal limits (Fig. 1*C*).

Case 2. M.S., a 62 year old female with known hypertension for several years, was admitted for hypertensive evaluation. Her blood pressure while in the hospital ranged from 130/90 to 160/90. A right renal biopsy was performed on November 15, 1962 and a left renal biopsy on November 21, 1962. A renal arteriogram on November 23, 1962 demonstrated an abnormal collection of contrast material in the mid-portion of the right kidney (Fig. 2*A*). This persisted into the nephrographic phase and early segmental venous drainage of this area was present (Fig. 2*B*). These findings were consistent with an arteriovenous fistula.

A repeat arteriogram 20 months later on July 24, 1964 appeared normal (Fig. 2*C*). The arteriovenous fistula was considered healed.

Case 3. M. W., a 63 year old female with known hypertension for 10 years, was admitted for study in 1963. Her blood pressure ranged from 148/84 to 210/110. An unsuccessful right renal biopsy was attempted on April 19, 1963. Right renal biopsy was successful on April 22, 1963 under television image amplifier



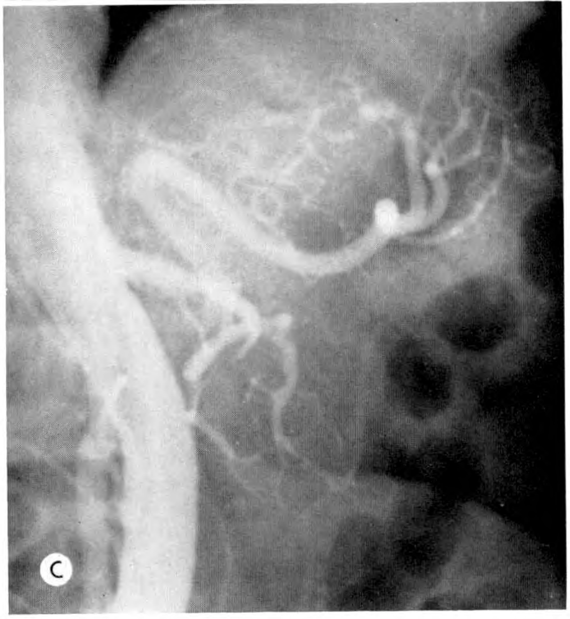


Fig. 1. Case 1. (*A*) Initial renal arteriogram, arterial phase. Pooling of contrast medium in left lower pole diagnostic of arteriovenous fistula (←). Note enlargement of lower pole due to intra- or peri-renal hematoma. (*B*) Late arterial phase. Large venous drainage trunk (↗). (*C*) Renal arteriogram 3 months later, arterial phase. No arteriovenous fistula present. The lower pole configuration appears normal.

control. Left renal biopsy was done on April 26, 1963. No complications post biopsy were noted.

Renal arteriograms on April 30, 1963 demonstrated an arteriovenous fistula in the lower pole of the left kidney (Fig. 3, *A* and *B*). A repeat arteriogram, 16 months later, outlined the persistent arteriovenous fistula (Fig. 3*C*). This appeared smaller than on the initial study and presumably represented partial healing.

Case 4. H.J., a 39 year old male with known hypertension for several years, was admitted for hypertensive study in 1963. He had a blood pressure range of 116/78 to 220/130. Right renal biopsy was done on March 16, 1963 and left renal biopsy on March 22, 1963. No complications followed either biopsy other than the transient presence of a few red blood cells in the urine following left renal biopsy.

The renal arteriogram of March 25, 1963 showed an arteriovenous fistula involving the mid-portion of the left kidney (Fig. 4*A*) with typical abnormal pooling and with demonstration of the venous drainage (Fig. 4*B*).

The patient was re-admitted in 1964 for re-evaluation of his hypertensive status. A second renal arteriogram on February 5, 1964 showed persistence of the arteriovenous fistula (Fig. 4*C*). The degree of opacification at the fistulous site was not as good as that noted 11 months previously.

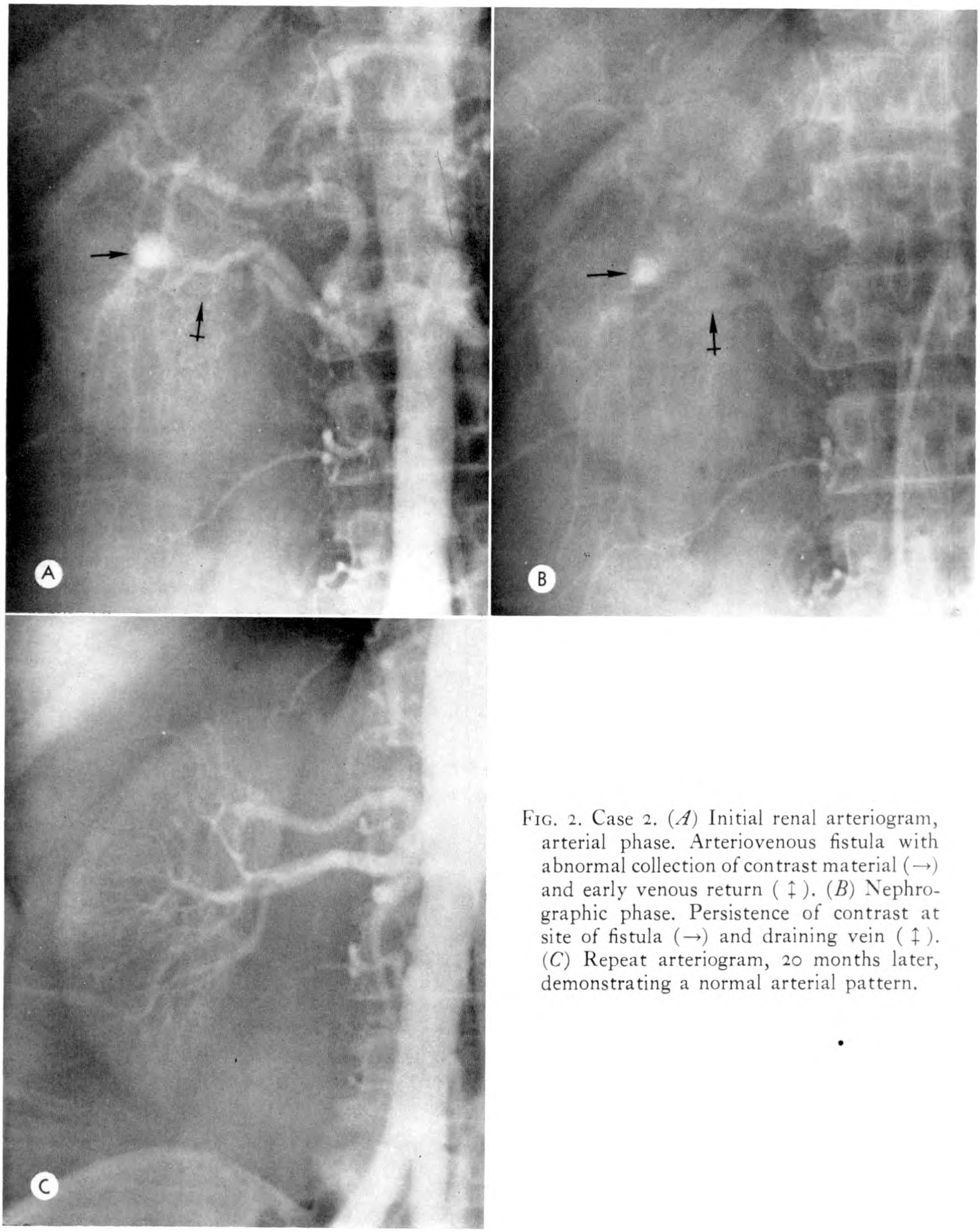


FIG. 2. Case 2. (*A*) Initial renal arteriogram, arterial phase. Arteriovenous fistula with abnormal collection of contrast material (→) and early venous return (↨). (*B*) Nephrographic phase. Persistence of contrast at site of fistula (→) and draining vein (↨). (*C*) Repeat arteriogram, 20 months later, demonstrating a normal arterial pattern.

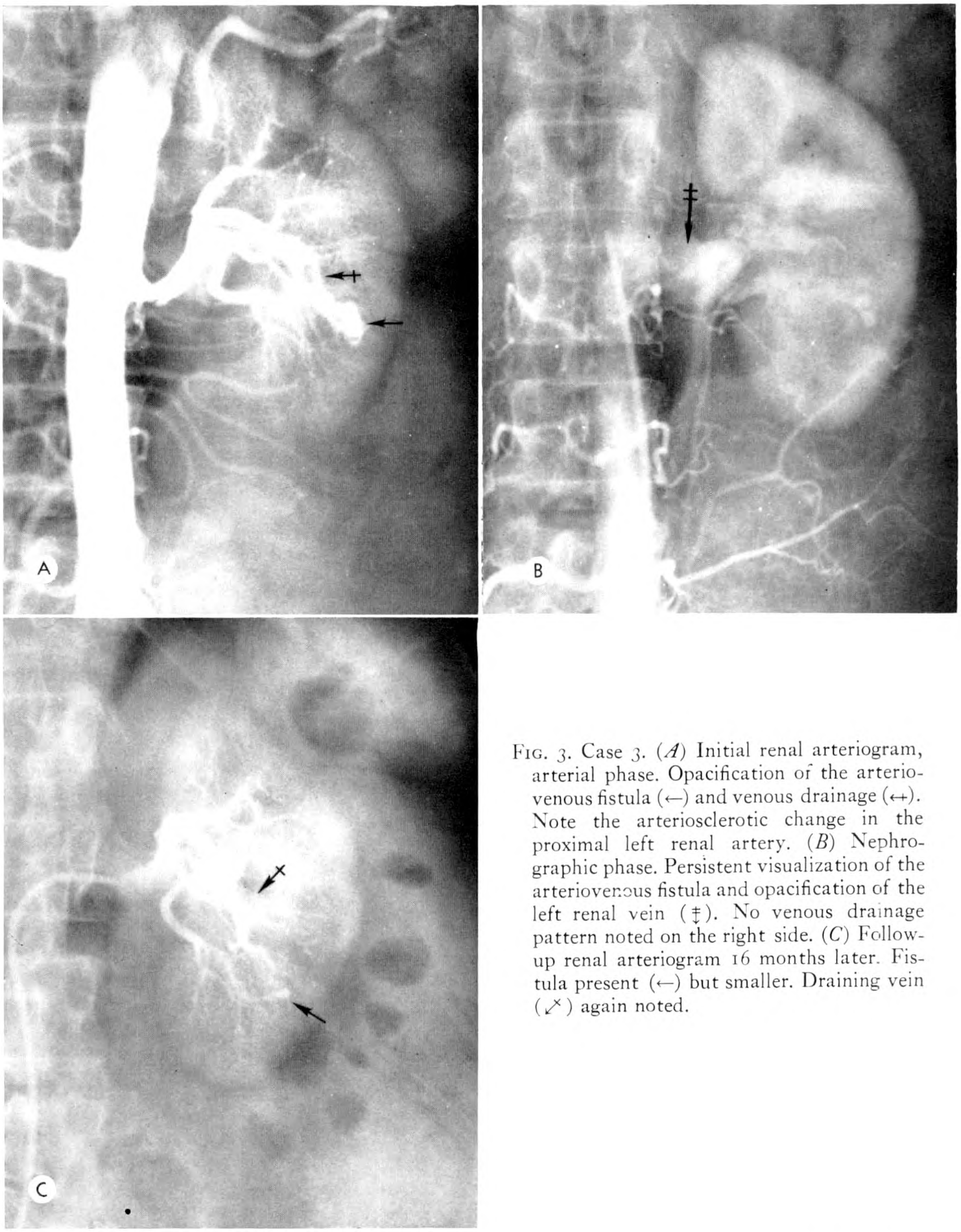


FIG. 3. Case 3. (*A*) Initial renal arteriogram, arterial phase. Opacification of the arteriovenous fistula (←) and venous drainage (↔). Note the arteriosclerotic change in the proximal left renal artery. (*B*) Nephrographic phase. Persistent visualization of the arteriovenous fistula and opacification of the left renal vein (‡). No venous drainage pattern noted on the right side. (*C*) Follow-up renal arteriogram 16 months later. Fistula present (←) but smaller. Draining vein (↙) again noted.

CASE 5. B.B., a 57 year old female, was admitted for hypertensive evaluation. Her blood pressure ranged from 110/78 to 208/120. Renal arteriograms made on June 14, 1963 showed no abnormality of the renal arteries (Fig. 5*A*).

The patient was re-admitted in 1964 for re-evaluation and further studies. On March 2, 1964, a right renal biopsy was done and on March 9, 1964 a left renal biopsy was performed, both without complication. A repeat renal arteriogram on March 4, 1964 showed an arteriovenous fistula in the mid-portion of the right kidney with typical irregular pooling of contrast material during the arterial phase and with rapid opacification of the draining vein (Fig. 5*B*).

Persistence of the arteriovenous communication was again demonstrated on a repeat

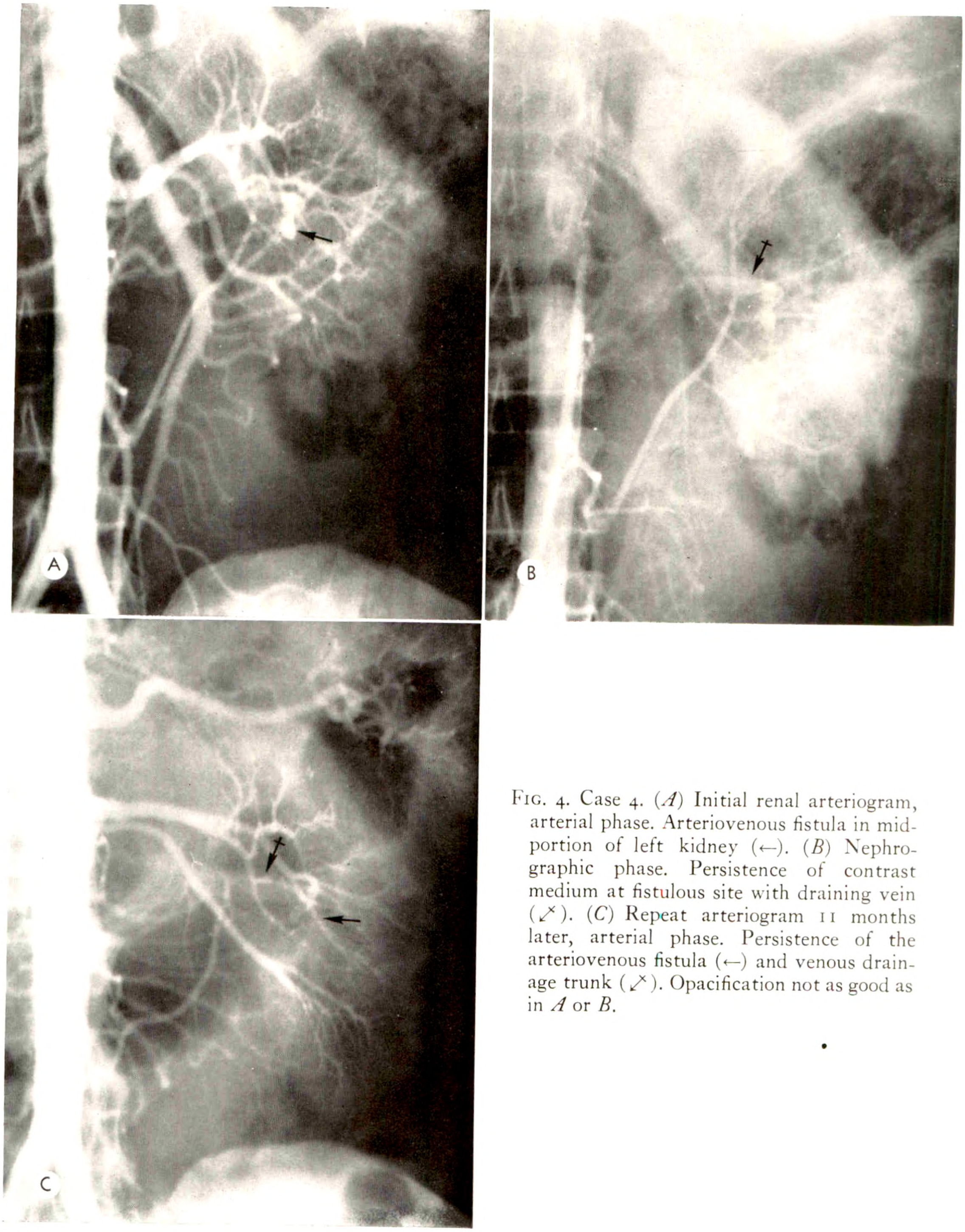


FIG. 4. Case 4. (*A*) Initial renal arteriogram, arterial phase. Arteriovenous fistula in mid-portion of left kidney (←). (*B*) Nephrographic phase. Persistence of contrast medium at fistulous site with draining vein (↙). (*C*) Repeat arteriogram 11 months later, arterial phase. Persistence of the arteriovenous fistula (←) and venous drainage trunk (↙). Opacification not as good as in *A* or *B*.

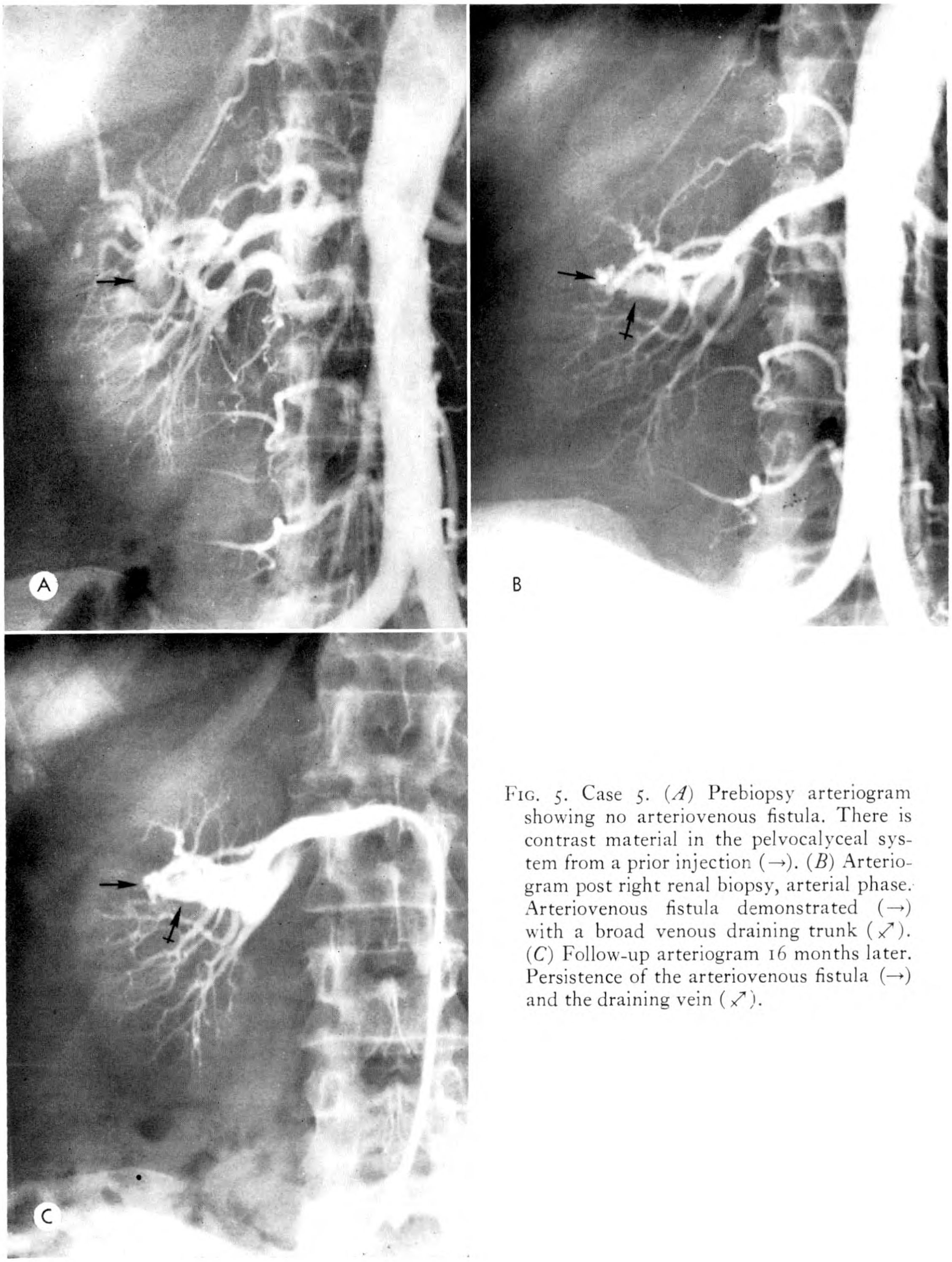


Fig. 5. Case 5. (*A*) Prebiopsy arteriogram showing no arteriovenous fistula. There is contrast material in the pelvocalyceal system from a prior injection (→). (*B*) Arteriogram post right renal biopsy, arterial phase. Arteriovenous fistula demonstrated (→) with a broad venous draining trunk (↗). (*C*) Follow-up arteriogram 16 months later. Persistence of the arteriovenous fistula (→) and the draining vein (↗).

arteriogram on July 24, 1964, 16 months after the initial study (Fig. 5*C*). No significant difference was demonstrated in the appearance of the fistula.

CASE 6. J.C., a 36 year old female with known hypertension since the age of 14 years, was admitted in March, 1964 for hypertensive study. Her blood pressure ranged from 170/110 to 200/130. An intravenous pyelogram on March 12, 1964 showed no abnormality of the pelvocalyceal systems (Fig. 6*A*). A renal arteriogram on March 13, 1964 showed no abnormality of the renal arteries or their intrarenal branches (Fig. 6*B*). Right renal biopsy was performed on March 17, 1964 without apparent complication.

The patient was re-admitted in May, 1964 for left renal biopsy and re-study. A repeat intravenous pyelogram on May 29, 1964 showed a pressure defect on the right renal pelvis and middle calyceal group (Fig. 6*C*). Selective right renal arteriograms on May 29, 1964, revealed a rounded collection of contrast material pooled at the site of the abnormality seen on the intravenous pyelogram (Fig. 6, *D* and *E*). The pooling persisted on the sequential roentgenograms, lasting for 35 seconds. No venous drainage was visualized. The findings were considered diagnostic of an aneurysm.

ROENTGENOGRAPHIC FINDINGS

The salient points in the roentgenographic diagnosis of arteriovenous fistula and aneurysm are:

1. Arteriovenous fistula:
   a. Irregular pooling of contrast material in the course of an intrarenal branch artery.
   b. Early segmental venous opacification during the arterial or early nephrographic phase communicating with the localized collection.
2. Aneurysm:
   a. Early fill of a localized, smooth pocket of contrast material during the arterial phase.
   b. Persistent contrast visualization into late phases of the serialographic run, up to 10 to 30 seconds.
   c. Absence of venous drainage.

DISCUSSION

The common denominator to all arteriovenous fistulae and false aneurysms appears to be destruction of the arterial wall. Damage to an arterial wall may result from percutaneous renal biopsy. If there is simultaneous venous damage, or if the hematoma that results eventually communicates with a renal vein, fistula formation ensues.

It is probable that arteriovenous fistulae are more common than their reported incidence. Twigg *et al.*[22] were able to locate 26 previous cases. Trauma,[2,6,10,14,18] neoplasm,[1,16] renal surgery,[7,13,15,19] and congenital malformations[6,11,17] constitute the majority of previously reported cases. Percutaneous renal biopsy has been implicated in only a few case reports.[3,4,9] Fernstrom and Lindblom[9] described 1 case that they attributed to closed renal biopsy. Following discovery of this case, they made arteriograms on 20 additional patients post biopsy, but failed to uncover further cases. Blake *et al.*[3] described the angiographic and clinical features of 2 additional cases. These had detectable bruit. Sixty other cases in their series were considered free from fistula formation because no murmurs were heard. They concluded that the failure of detectable bruit could "probably be accepted as good evidence of the absence of arteriovenous fistula of the kidney."

Kark *et al.*[12] report the total incidence of complications in percutaneous renal biopsy as 9.8 per cent. Other workers have approximated this complication rate. Most of these complications were minor and did not require specific therapy. Neither Kark *et al.*[12] nor Brun and Raaschou[5] make mention of arteriovenous fistula as a complication. Slotkin and Madsen[21] evaluated by questionnaire the complication rate of 5,000 renal biopsies. One case of arteriovenous fistula between the intercostal vessels is reported, but none involved the kidney. Apparently, none of these series had routine or selected post-biopsy arteriograms.

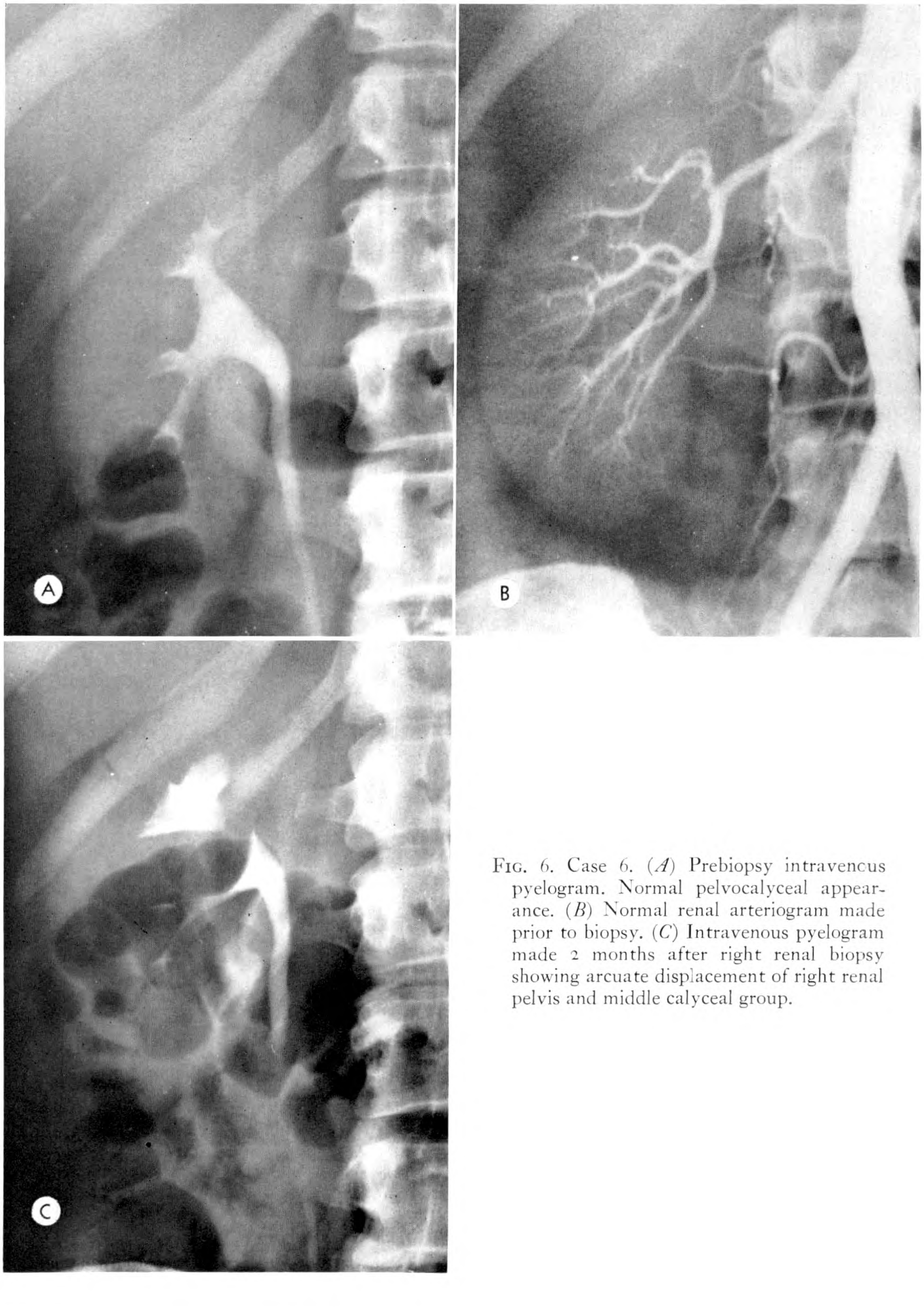


Fig. 6. Case 6. (*A*) Prebiopsy intravenous pyelogram. Normal pelvocalyceal appearance. (*B*) Normal renal arteriogram made prior to biopsy. (*C*) Intravenous pyelogram made 2 months after right renal biopsy showing arcuate displacement of right renal pelvis and middle calyceal group.

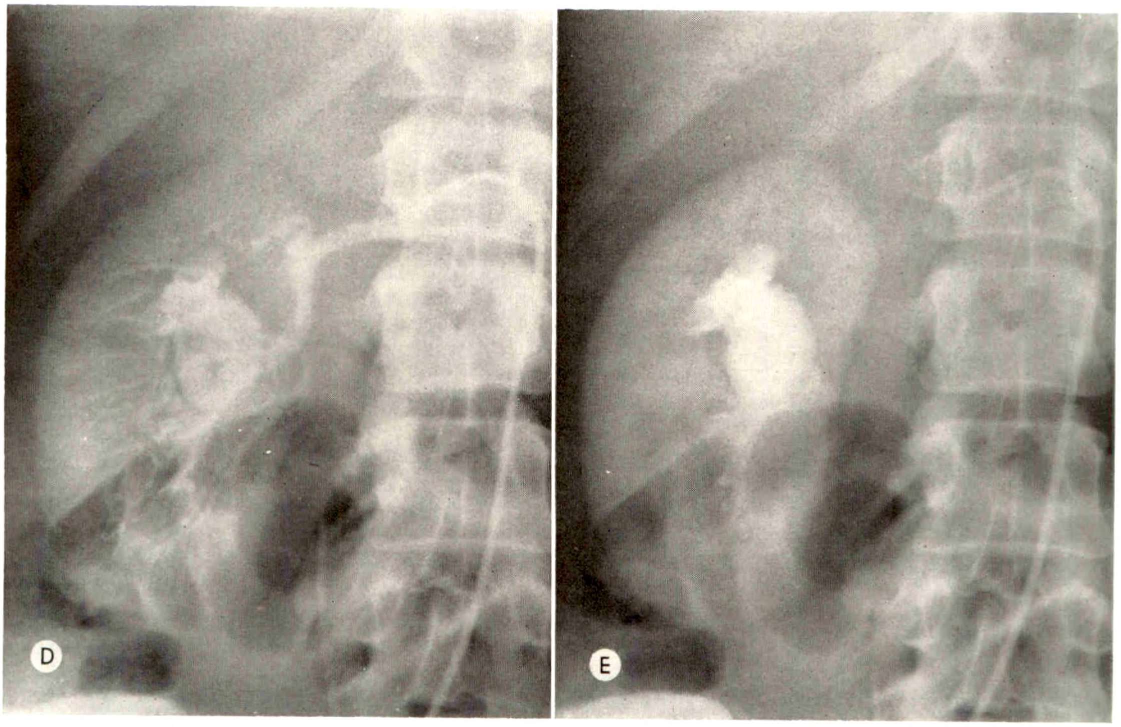


Fig. 6. (*D* and *E*) Selective right renal arteriograms made the same day as *C*. Aneurysm corresponding to abnormality demonstrated by urogram. No venous drainage seen. (*D*) Arterial phase; (*E*) nephrographic phase.

In this series, the 11 vascular abnormalities were found only in the group having biopsy prior to arteriography. No similar alteration was encountered in the group having arteriography prior to biopsy. This incidence is higher than has been recognized previously. However, other than the series described by Fernstrom and Lindblom,[9] no comparable post-biopsy arteriographic study has been made.

There has been no apparent significant alteration in the clinical course and evolution of the hypertensive process in these 11 patients to date. As demonstrated by the follow-up studies (Table II), 3 arteriovenous fistulae have healed, 1 arteriovenous fistula has shown partial healing, and 2 have persisted. One aneurysm has become smaller. No case yet encountered has shown an increase in the size of the abnormality within the follow-up period.

Judging from the size and peripheral location of these lesions and by the case histories of the involved patients, an arteriovenous fistula or aneurysm may be present without symptomatology. Any patient who develops renal symptomatology and/or urographic changes following renal biopsy should be suspected of harboring an arteriovenous fistula or aneurysm. Arteriography can be performed to prove the diagnosis.

SUMMARY AND CONCLUSIONS

In a group of 58 hypertensive patients undergoing renal arteriography following percutaneous renal biopsy, 11 cases of intrarenal arteriovenous fistulae and aneurysms were encountered. This would indicate a higher incidence of this complication than has been recognized previously. Healing, complete or partial, was demonstrated in 5 out of the 7 patients available for follow-up examination. Arteriographic studies would appear to be necessary for proper recognition.

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VOL. 95, NO. 2

RENAL AORTOGRAPHY*

ADVANTAGES AND TECHNIQUE USING THE VALSALVA MANEUVER

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RENAL aortography has become accepted as the procedure of choice for evaluating the patient with possible renovascular hypertension.[4,10] Up to 38 per cent of hypertensive patients, of whom 43 per cent were under 40 years of age, have been shown to have surgically remediable occlusive renal artery disease.[3] Other renovascular causes of hypertension, frequently curable by surgical intervention, include thrombotic and embolic phenomena, aneurysms and arteriovenous malformations.

In addition to the surgically correctable renovascular lesions, aortography will demonstrate renal parenchymal diseases which may result in hypertension. These include arteriolar nephrosclerosis and pyelonephritis. If the extent of the disease process can be shown to be limited mainly to one kidney, nephrectomy usually results in a complete remission of the hypertensive condition.

The other major indication for renal aortography is in differentiating benign from malignant kidney masses and in identifying those masses which are actually extrarenal, such as adrenal tumors. Spurious kidney masses resulting from malrotation and fetal lobulation are best substantiated by renal aortography.

The value of renal vascular contrast studies for planning a surgical procedure or long term medical management is inestimable. In this paper a technique of renal aortography utilizing the Valsalva maneuver, which results in maximal flooding of the aorta with contrast material and produces superior definition of all the renal vasculature, is described. An intense early and late nephrogram effect is obtained. The effect of the Valsalva maneuver on systemic pressure and cardiac output has been determined in 17 patients. This method of renal aortography has been performed in 583 patients. In no instance has selective renal arteriography been required. Some of the advantages of renal aortography are roentgenographically documented.

TECHNIQUE

Of the 583 patients undergoing renal aortography, the percutaneous retrograde transfemoral technique described by Seldinger[11] was successfully used in 572 cases (98.1 per cent). The remaining 11 patients were subsequently examined using translumbar aortography. However, the Valsalva maneuver was used for all examinations and 40 to 45 cc. of contrast material* was mechanically injected in all instances. Eight kg./cm.^{2} of pressure was used for the percutaneous retrograde injections and 5 kg./cm.^{2} for the translumbar injections.

A 65 cm. straight gray Ödman catheter, tapered for the small 160 guide and containing 4 to 6 large side-holes, was passed to the level of L1–L2. Occasionally (4 per cent of patients), a red Ödman catheter was used to negotiate very tortuous iliac arteries. The left common femoral and iliac arteries have proved to be easier to catheterize in patients with advanced arteriosclerosis since they are a more direct continuation of the aorta. Except for difficult cases, the catheter was advanced to the proper position without fluoroscopy. A test roentgenogram was made to check catheter position and to determine roentgenographic technique. If patient size permitted, the lateral edges of the Schönander camera were covered with lead rubber strips to help eliminate scatter.

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* Renografin 60%, E. R. Squibb & Sons, New York. Hypaque 50%, Winthrop Laboratories, New York.

* From the Department of Radiology, University of Missouri Medical Center, Columbia, Missouri.

The patient is carefully instructed on how to perform a Valsalva maneuver. After the importance of the Valsalva maneuver to a successful examination is explained to the patient, full cooperation is almost always obtained. Before the actual examination is made, the patient practices the described sequence of events two or three times.

The patient takes in a deep breath and strains as hard as possible against the closed glottis. After the Valsalva maneuver has been maintained for 8 to 10 seconds, the filming sequence of 3 films per second for 3 seconds and 1 film per second for 6 seconds is started. Since there is approximately a 1 second delay for the Schönander camera to expose the first film, there is a 1 second pause before the contrast material is injected. After the first 9 films have been exposed, the patient is told to "exhale." Breathing is not permitted until the last 6 films have been exposed. The films are processed and checked immediately to see if oblique views are needed to further delineate a questionable finding. Upon termination of the study, the catheter is removed and manual pressure is applied over the arterial puncture site (not over the small skin incision) for at least 10 minutes or until bleeding is completely controlled.

DISCUSSION OF TECHNIQUE

The systemic pressure changes produced by the Valsalva maneuver were measured in 17 patients using a pressure transducer connected to the catheter positioned at the L1–L2 level. Pressures were continuously recorded before, during and after the Valsalva maneuver. Each patient also had a right heart catheterization and the cardiac output before the Valsalva maneuver and after 9 to 10 seconds of sustained straining was determined using the Fick principle.[7]

Figure 1 is a representative aortic pressure tracing. Upon initiation of the Valsalva maneuver, there is a transient rise in systemic pressure due to blood being forced out of the lungs and left heart, secondary to increased intrathoracic and intra-abdominal pressure. However, within 1 or 2 seconds, the systemic pressure starts to fall and reaches a plateau in 7 or 8 seconds. This fall in pressure results from decreased venous return to the heart. In the 17 patients, the average decrease produced in systolic pressure by the Valsalva maneuver was 52 per cent of the resting pressure. The average diastolic pressure was reduced by 30 per cent over the resting value. The increased pressure applied to all the intra-

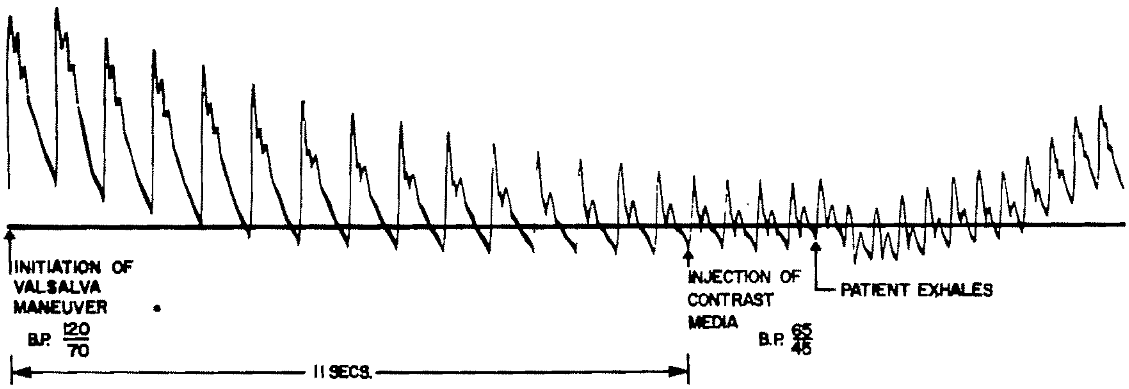

Fig. 1. The systemic pressure changes produced by the Valsalva maneuver are recorded through a catheter at the level of the renal arteries. The technique of renal aortography as related to these physiologic changes is indicated on the graph. This patient's cardiac output was reduced by 46 per cent after 9 seconds of straining.

thoracic cardiovascular structures and the impeded venous return to the heart result in a diminished cardiac output.[8] The reduction in cardiac output averaged 48 per cent of the resting output in the 17 patients.

Contrast material is injected after 8 to 10 seconds of sustained straining when the systematic pressure and cardiac output have been maximally decreased. This results in flooding the aorta with relatively undiluted contrast material. In the supine position, the renal arteries are dependent as compared to the other major arteries arising from the abdominal aorta. The slow flow of contrast medium produced by the Valsalva maneuver enhances the filling of the renal arteries as does the layering effect of the heavy contrast material. For these reasons, the renal arteries are best demonstrated on the initial 3 or 4 films (Fig. 2), and thus the film sequence should be started slightly ahead of the injection of contrast material so that the very early filling of the renal arteries is not missed.

After the initial 9 films have been exposed, the patient exhales. This is associated with a transient drop in systemic pressure due to blood rushing into the empty pulmonary bed. Two or three seconds later, there is an "over-shoot" of both systemic pressure and cardiac output followed by a return to normal pressure. The "over-shoot" phenomenon helps to maintain the peripheral flow of the bolus of contrast material into the renal arterioles, producing an intense nephrogram.

ADVANTAGES

Renal aortography utilizing the Valsalva maneuver produces superior demonstration of the kidney vasculature because the decreased systemic pressure and cardiac output allow a greater bolus of undiluted contrast material to be delivered to the renal arteries. The straightening of the renal arteries, which occurs with the caudad shift of the kidneys during the Valsalva maneuver, is important for differentiating fibromuscular hyperplasia[9] from arteriosclerotic plaques and tortuosity. Upon exhalation, the kidneys should return cephalad to their normal position.

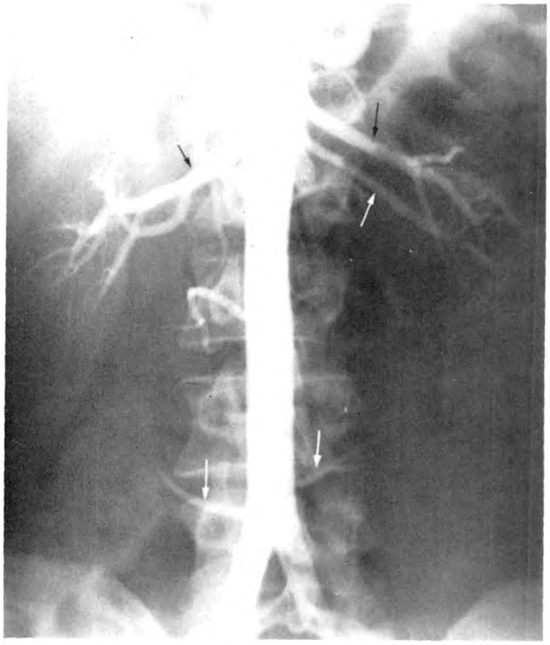

FIG. 2. Roentgenogram exposed 1 second after start of injection with very good unobstructed demonstration of 5 renal arteries. The interlobular renal arteries are starting to fill.

The described technique of renal aortography is the procedure of choice in evaluating renal masses. Figure 3, *A* and *B* shows a normotensive 36 year old white female in whom a mass in the left kidney was demonstrated on intravenous urograms. The renal aortogram demonstrated the mass to be a very large cyst. In addition, there was fibromuscular hyperplasia of the right renal artery. The presence of the potential hypertensive lesion involving the right renal artery caused the surgeons to be doubly careful in marsupializing the cyst of the left kidney. Figure 4, *A* and *B* shows a 41 year old female whose intravenous pyelogram demonstrated a mass in the right kidney, probably a cyst. The renal aortogram confirmed the presence of the cyst of the right kidney and demonstrated an unsuspected cyst of the left kidney. The surgeons altered their approach when the additional lesion in the opposite kidney was found. The identifica-

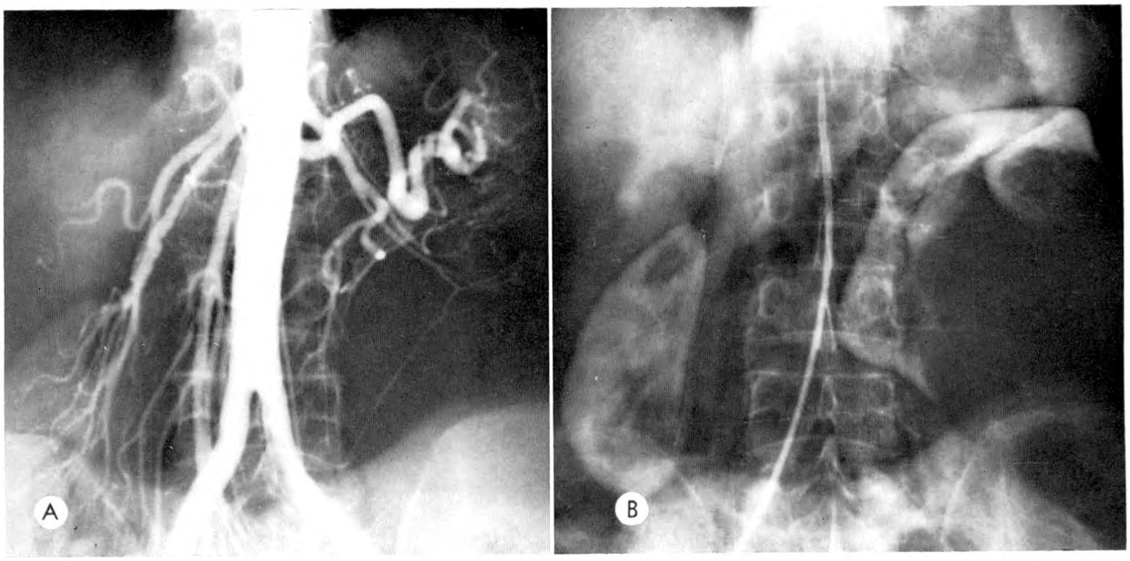

Fig. 3. Normotensive patient whose intravenous pyelogram showed a mass in the left kidney. (*A*) Complete flooding of the aorta is present on the aortographic film exposed at 1 second. There is unsuspected typical fibromuscular hyperplasia involving the renal artery to a ptotic right kidney. The inferior branches of the left renal artery are stretched around an avascular mass. (*B*) Late nephrogram showing displacement and distortion of the left renal tissue. Splenic and portal veins are opacified as is the right renal vein.

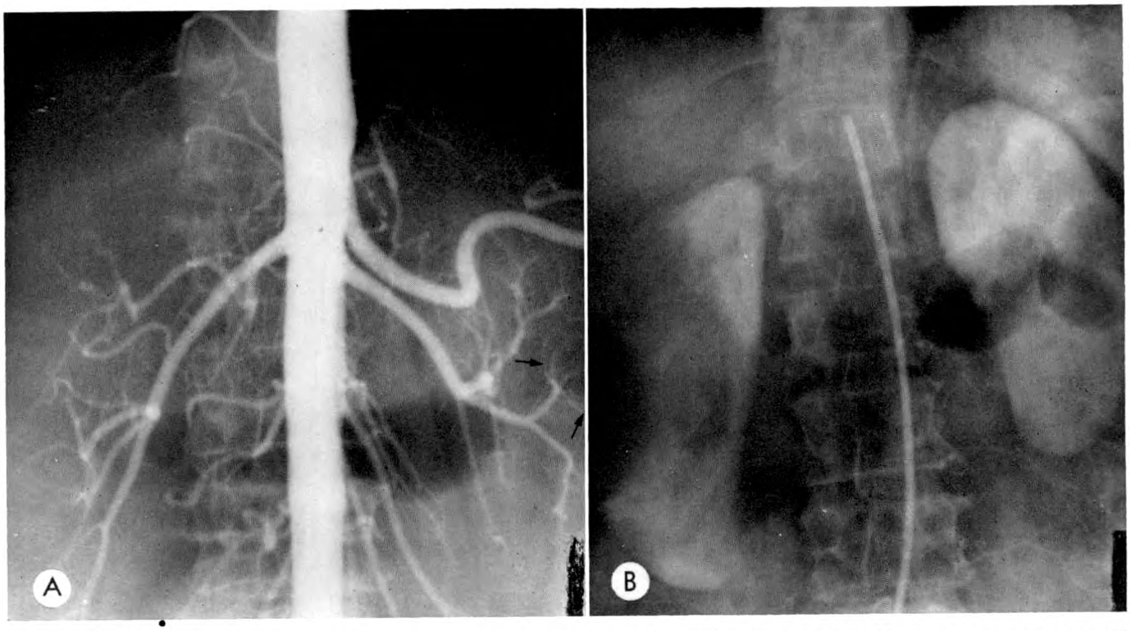

Fig. 4. The intravenous pyelogram demonstrated a mass in the right kidney. (*A*) Early roentgenogram ($\frac{2}{3}$ second after injection) demonstrates excellent renal artery anatomy. There is stretching and displacement of the right renal artery branches. There is localized distortion of the renal arteries in the mid-peripheral portion of the left kidney. (*B*) Nephrogram exposed at 7 seconds shows a huge cyst of the right kidney and an unsuspected 5 cm. cyst of the left kidney.

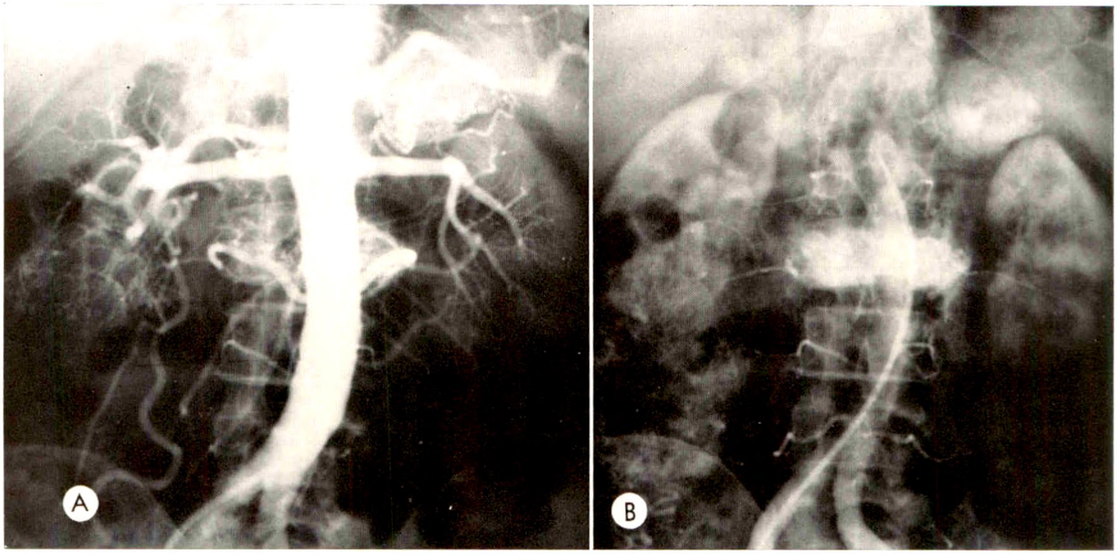

Fig. 5. Intravenous pyelogram showed a probably malignant tumor of the right kidney. (*A*) There is excellent opacification of the renal arteries on a film exposed $\frac{2}{3}$ second after injection of contrast medium. Tumor vessels are identified in the lower pole of the right kidney. In addition, unsuspected metastases are identified by tumor vessels in both adrenals and the third lumbar vertebral body. (*B*) Roentgenogram obtained 3 seconds after injection gives very good definition of the large right renal cancer and the metastases.

tion of previously undetected cysts in the opposite kidney by renal aortography has occurred in 9 cases in the series.

Malignant renal lesions should always be examined by renal aortography. Figure 5, *A* and *B* is that of a 67 year old male. Intravenous pyelograms showed a tumor, probably malignant, involving the right kidney. Renal aortography using the Valsalva maneuver provided excellent detail of a large necrotic tumor. Of greater significance was the demonstration of unsuspected metastases to both adrenals and the third lumbar vertebral body. In 5 cases of kidney carcinoma in this series, previously unidentified metastases have been depicted by renal aortography. The patients were thereby saved needless surgery.

Renal aortography, utilizing the Valsalva maneuver, produces excellent filling of the main renal arteries on the early roentgenograms followed by demonstration of the parenchymal interlobular and cortical arteries and the nephrogram on later films. The use of selective renal arteriography with its inherent hazards[5,6] is unnecessary. Unsuspected metastatic disease, vascular pathology, and lesions involving the other kidney will not be detected if only selective renal arteriography is used. Renal aortography is indicated prior to any renal surgery to demonstrate possible supernumerary arteries and other kidney anomalies (Fig. 2).[1,12]

In this series the only significant complication occurred during one of the translumbar examinations. About 10 to 15 cc. of contrast material was injected intramurally. The patient experienced severe pain for about 15 minutes but the pain had completely subsided within 1 hour. There were no sequelae.

The enhanced delivery and flow of contrast material produced by the Valsalva maneuver are used by the author in the examination of many other vascular regions. These include the distal aorta and both the iliofemoral arterial systems[3] and the thoracic aorta, particularly the brachiocephalic arteries.

CONCLUSION

A technique for renal aortography utilizing the Valsalva maneuver is described. The decrease in systemic pressure and cardiac output produced by the Valsalva maneuver has been determined in 17 patients. The injection of contrast material at the peak of these alterations in cardiovascular physiology results in excellent filling and detail of the renal arteries and an intense nephrogram. Selective renal arteriography has not been required in the 583 patients examined.

Renal aortography using the Valsalva maneuver is the examination of choice for all patients with possible renovascular hypertension, for those patients undergoing renal surgery and for patients with a mass in or around the kidneys. Not infrequently, unsuspected mass lesions are identified in the other kidney or metastases are demonstrated which significantly alter the management of the patient.

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THE RADIOLOGIST AND THE PROBLEM OF RENAL VASCULAR HYPERTENSION[*]

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THE publication in 1934 of Goldblatt and co-workers'[16] classic experiments dealing with the production of hypertension in dogs by bilateral constriction of the renal arteries focused attention on the role of renal ischemia in this disease. Before long, experimental hypertension was described in other species by numerous investigators using a variety of techniques which decreased arterial flow to one kidney.

Enthusiasm for the surgical cure of hypertension due to unilateral renal disease in man was stimulated by Butler's[9] report in 1937 of a successful outcome following nephrectomy in 2 patients with pyelonephritis. Unfortunately, the early optimism engendered by this report has not been universally substantiated in the ensuing years. In 1948, Smith[46] highlighted the over-all disappointment in a review of the results of unilateral nephrectomy for hypertension in various centers throughout the United States. It is evident from these data that only about 19 per cent of patients subjected to nephrectomy had significant lasting relief of their hypertension.

More recently, necropsy and *in vivo* arteriographic studies have shown that renal arterial stenosis is relatively common in normotensive as well as in hypertensive patients above the age of 50 years.[12,21,28] Thus, Holley and his associates at the Mayo Clinic,[21] in a review of 294 unselected necropsies reported moderate or severe renal arterial stenosis in 12 per cent of normotensive patients under the age of 50 years and 64 per cent of such patients over 50 years of age. In view of these findings, the demonstration of renal arterial stenosis does not necessarily mean that the arterial lesion is the cause of the patient's hypertension. Present estimates indicate that about 5 to 15 per cent of hypertensive patients have a renal vascular basis for their hypertension.[34,40] In this dilemma, how can the radiologist help select the hypertensive patient with renal vascular disease who is likely to benefit from surgical intervention?

The answer to this question must be sought in an analysis of the currently accepted hypothesis of the etiology of renal vascular hypertension and of the pathophysiologic characteristics of the involved kidney.

1. Renal arterial constriction causes a decreased mean perfusion pressure which in turn produces a reduction in the volume of glomerular filtrate in the involved kidney.[45b] However, the tubules go on resorbing sodium and water as though the volume of glomerular filtrate were normal. This results in excessive resorption of sodium and water, principally in the proximal convoluted tubule but also in the distal tubule.[4,5,7,8,24,37,39,44,47]

2. Although the exact mechanism underlying the production of renal vascular hypertension in man has not been thoroughly established as yet, a number of investigators have proposed the following attractive hypothesis (Fig. 1). A fall in renal mean arterial perfusion pressure decreases the stretch of the afferent arteriole.[45b] This, in turn, stimulates hyperplasia of the juxta-glomerular cells interposed between the macula densa of the distal tubules and the lumen of the afferent arteriole, with a concomitant increase in renin activity. The proteolytic enzyme renin acts on renin precursor, an alpha-2-globulin elaborated in the liver, to split off a physiologically inert decapeptide (angiotensin 1).

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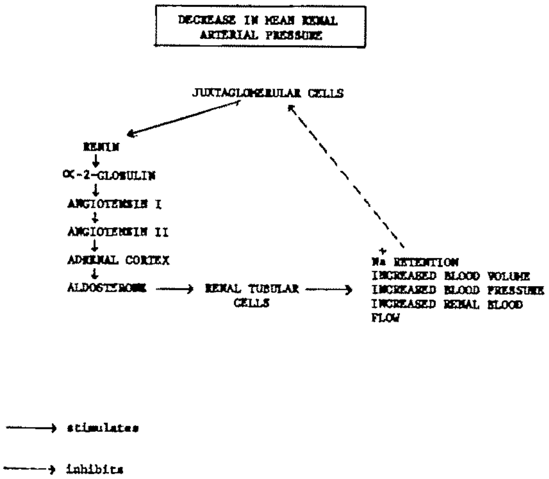

Fig. 1. Hypothetical model of normal negative feedback control mechanism.

A second specific plasma enzyme acting on angiotensin I splits off two amino acid groups to form an octapeptide, angiotensin II, which has marked vasopressor properties. Angiotensin II stimulates aldosterone secretion in the zona glomerulosa of the adrenal cortex. The aldosterone acts on the renal tubular epithelium to promote sodium and water resorption, thereby increasing blood volume, mean renal arteriolar pressure and, in turn, decreasing the juxta-glomerular cellular granularity and renin formation.[16,17,18,19,50] In essence, there is postulated a delicate feedback control system in which the juxta-glomerular cells appear to act as pressure receptors responding to changes in renal arteriolar pressure.

How can the radiologist utilize this information to cooperate in the design of a profile of diagnostic procedures which will detect (1) reduced renal mean arterial pressure and (2) the unique ability of the abnormal kidney to resorb excessive amounts of sodium and water?

I. INTRAVENOUS PYELOGRAPHY

Since the diatrizoate compounds are almost entirely excreted by glomerular filtration, an intravenous pyelography performed with these media may be regarded as a roentgenographic plasma inulin clearance test.[31,35] For practical purposes, one may assume that once the diatrizoate compound filters through the glomeruli into the tubules, no significant addition or subtraction of this material by tubular resorption or secretion occurs. Hence, the plasma clearance of the diatrizoate compound may be said to represent the glomerular filtration rate. The difference between the diatrizoate concentration in the plasma (and glomerular filtrate) and its final concentration in the urine must be due to reabsorption of water in the tubules.

A fall in mean arterial pressure to one kidney, due either to constriction of the main renal artery or to more peripheral narrowing, results in the delayed arrival of a smaller volume of contrast medium and a reduction in glomerular filtrate—factors which tend to produce decreased renal opacification. Conversely, the reduced urinary flow rate of the abnormal kidney and the latter's unique ability to resorb excessive quantities of sodium and water produce a relatively greater concentration of contrast medium, *i.e.*, increased renal opacification. The balance between these opposing forces will determine whether the abnormal kidney in a given patient is more, less or equally radiopaque compared with the normal side.

The failure to appreciate and exploit these pathophysiologic phenomena has led to the disrepute of intravenous pyelography in the diagnosis of renal vascular hypertension. Critics have justly said that classic intravenous pyelography is positive in only about 50 per cent of patients with this disease. Because of this deficiency, we proceeded early in 1962 to revise the technique of intravenous pyelography for screening hypertensive patients. We were then unaware that Liese[29] and also Rathe[41] had previously suggested nephrotomography for this purpose.

TECHNIQUE OF MODIFIED INTRAVENOUS PYELOGRAPHY

After considerable study and trial, the following procedure has been adopted for patients being screened for renal vascular hypertension. It is preferable that the patient not receive diuretics nor be on a salt-restricted diet for a week prior to the intravenous pyelography. This precaution obviates the possibility of a false negative due to sodium restriction. Under the latter circumstances, the excessive sodium reabsorption which distinguishes the ischemic from the normal kidney may not be evident since both kidneys will have an increased avidity for sodium.

1. A preliminary book of tomograms of the kidneys in the supine position is made to select the optimal section for visualization of the kidneys. A rolled-up sheet or blanket is placed below the patient's shoulders in an effort to have the coronal plane of the kidneys parallel to the coronal plane of the body since the lower pole of the kidney frequently lies anterior to the upper pole. Although this maneuver helps to correct the tilt of the renal axis in many patients, it is by no means always successful. Not infrequently, it is impossible to see both kidneys completely outlined on a single section.

2. No special effort is made to dehydrate the patient prior to examination. However, 1.0 ml. of antidiuretic hormone (ADH) in the form of surgical pitressin is given subcutaneously 15 to 20 minutes before the intravenous diatrizoate injection. This standard dose of exogenous ADH is used to promote maximal reabsorption of water in the distal tubules and collecting ducts since the endogenous ADH level may not necessarily be maximal at the time of examination. The above dosage has not produced any significant untoward side effects to date.

3. Using a short No. 18 gauge needle with a wide-bore syringe, 1.0 ml./kg. of 76 per cent renografin (or an equivalent dose of another diatrizoate compound) is injected as rapidly as possible. The injection time for the average patient weighing 70 kg. does not exceed 15 seconds. Since our largest wide-bore syringe has a capacity of 80 ml., the latter represents the largest volume injected. No ureteral compression is employed. Following completion of the diatrizoate injection, the hub of the needle is connected by a short length of sterile, disposable polyethylene tubing to a flask containing 500 ml. of 5 per cent glucose in water. The solution is adjusted to drip in as slowly as possible, *i.e.*, 3 to 4 drops per minute to keep the needle patent.

4. Fifteen seconds after completion of the diatrizoate injection, a second book of tomograms is obtained.

5. Single pyelographic exposures are then made at 1, 2, 3, 5 and 10 minutes post injection.[33] The first 4 exposures are made on 10×12 inch films and the last on a 14×17 inch film.

6. After the 10 minute pyelogram, 40 gm. of urea dissolved in 10 per cent invert sugar in water (93 ml. total volume) is introduced into the polyethylene tubing by a needle. The urea and glucose solutions are permitted to run in rapidly so that the entire volume is delivered within 15 minutes.[2,3,47] This part of the procedure is omitted in patients with evidence of cardiac failure. The rapid infusion of urea not infrequently produces severe transient headache and local vein pain. An isolated case of subdural hematoma following similar urea diuresis has been reported in the literature.[32]

7. Single pyelograms are made 5, 10, 15 and 30 minutes after starting the urea-glucose infusion. Occasionally, a 45 or even a 60 minute film is desirable.

Originally, we thought that the nephrotomographic sections would provide (a) information concerning the appearance time and density of the contrast medium as a measure of renal arterial flow, (b) information concerning the disappearance time of the nephrographic phase in both kidneys, pointing up differences in urinary flow rates, (c) better visualization of the renal outlines, permitting more accurate measurement of renal size and, (d) recognition of segmental renal infarction. In practice, however, nephrotomography did not live up to theoretic expectations. Significant differences in appearance time and density

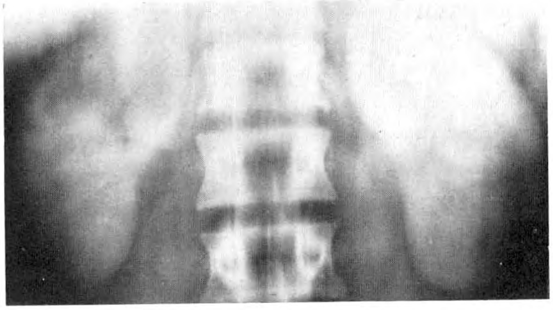

Fig. 2. Case i. Nephrotomogram showing intra-intestinal gas superimposed on the right kidney. Although multiple sections at 1 cm. levels were cut, the gas could not be satisfactorily eliminated.

of the nephrogram are not detectable in the presence of slight or moderate unilateral reduction of renal blood flow. It requires severe arterial stenosis to produce an unequivocal decrease in density on the nephrogram that the eye can detect. In addition, at times, insurmountable technical problems make it difficult to compare renal densities accurately, *i.e.*, high position of the right kidney producing a summation density of liver plus kidney, failure of multiple sections to eliminate overlying intestinal gas completely (Fig. 2). Nephrotomography does, however, provide better delineation of the renal outlines and the possibility of recognizing segmental renal infarction. In our experience, the significant findings associated with moderate reduction of renal blood flow to one kidney occur on the early pyelograms, *i.e.*, 1, 2 and 3 minute studies (Fig. 3; 4, *A* and *B*; and 5, *A* and *B*). These are (1) delayed appearance of the contrast medium in the pelvis and calyces of the abnormal kidney, reflecting the decreased glomerular filtration. This finding becomes more pronounced with increasing degrees of renal arterial constriction;[11,33] (2) increased radiopacity of the contrast medium in the pelvis and calyces due to excessive resorption of water and reduced urinary volume.[2] This abnormality may not be detected by the conventional dehydration technique of intravenous pyelography because both kidneys are then excreting a small volume of urine with high osmolality; and (3) in addition, the abnormal kidney, because of its propensity for

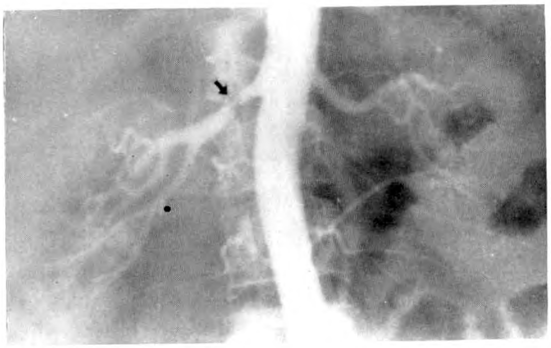

Fig. 3. Case ii. Aortogram demonstrating stenosis of the right renal artery.

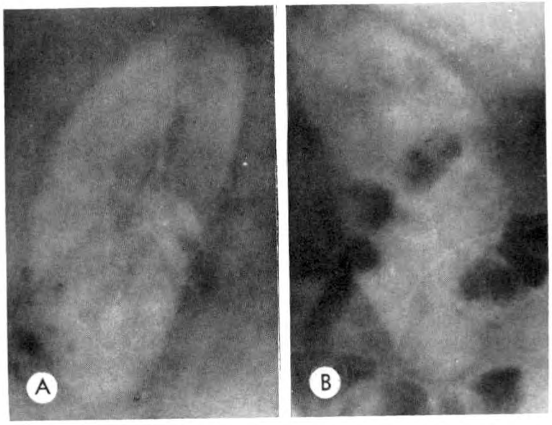

Fig. 4. Case ii. (*A* and *B*) Thirty second nephrotomograms showing equal opacification of both kidneys. The contrast medium in the left kidney pelvis is obscured by overlying gas in the bowel.

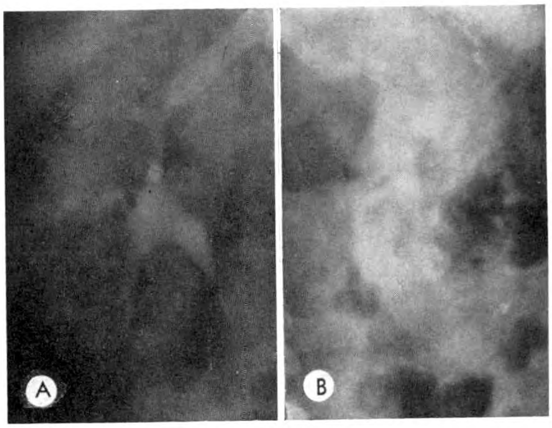

Fig. 5. Case ii. (*A* and *B*) Three minute intravenous pyelogram demonstrating increased density of the contrast medium in the collecting system of the abnormal right kidney.

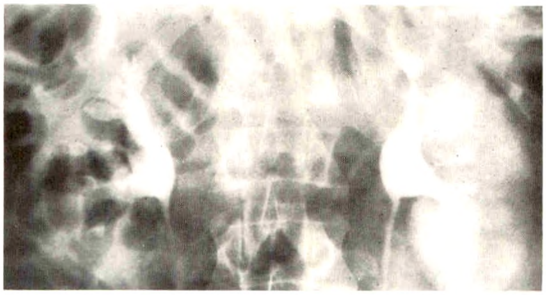

Fig. 6. Case iii. Intravenous pyelogram of a patient with mild hypertension and a normal aortogram prior to the administration of an osmotic diuretic.

excessive water resorption, is unable to wash out the contrast medium as efficiently as the normal side when subjected to forced osmotic diuresis. Hence, the pelvis and calyces of the abnormal kidney are more radiopaque than the normal side after a urea "wash-out."[1,2,42,47] This difference may not be apparent in the kidney with such marked arterial constriction that insufficient diatrizoate filters through the glomeruli to permit recognition of the excessive tubular water resorption. However, the latter type of kidney can readily be recognized by its considerably reduced size and the markedly delayed appearance time of the contrast medium in its pelvis-calyceal system. The authors have seen 2 false positive urea "wash-outs" which are not readily explainable (Fig. 6 and 7). In this connection, Amplatz[2] has also reported a few false positives due to a number of factors, *i.e.*, unilateral dilated renal pelvis, renal rotation, superimposed gas shadows, and unilateral transient contraction of the renal pelvis. Similarly, Schreiber *et al.*[42] recently noted an instance of false positive urea "wash out" and simultaneously corroborated the reliability of the negative reaction.

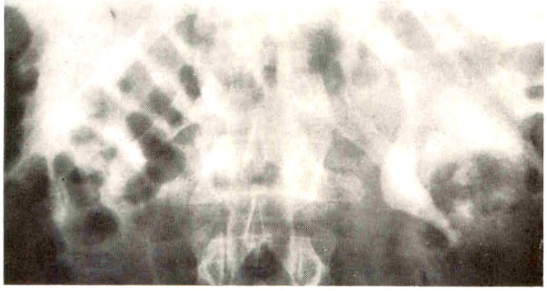

Fig. 7. Case iii. Intravenous pyelogram after forced osmotic diuresis showing a false positive urea "wash out" on the right side.

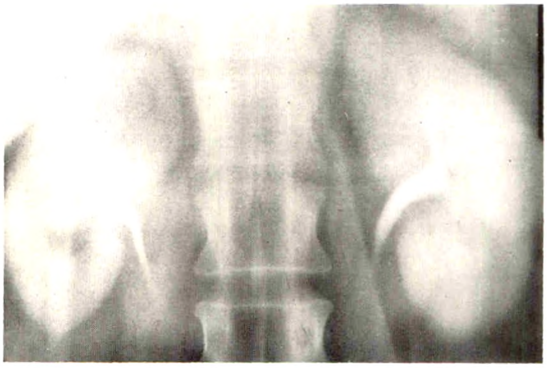

Fig. 8. Case iv. Late nephrotomographic phase of intravenous pyelogram with a normal appearance time of the contrast medium in both collecting systems. The right kidney is 2 cm. shorter than the left.

Any of these 3 findings, alone or in concert, is considered abnormal.

A significant disparity in renal length greater than 1 cm. is repeatedly stressed in the literature as a reliable index of unilateral renal artery stenosis. In our experience, this criterion *per se* has not proved to be as reliable as the modified intravenous pyelogram and isotopic renogram (Fig. 8 and 9).

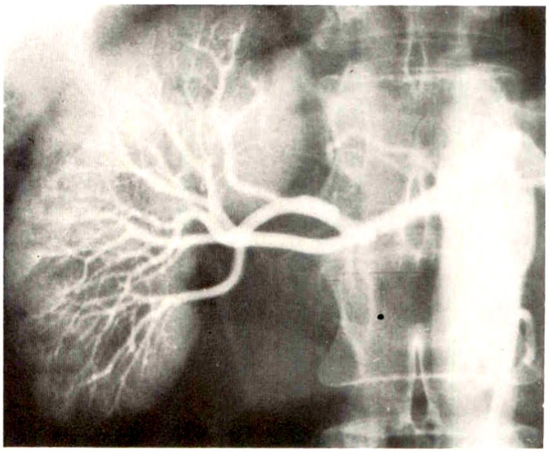

Fig. 9. Case iv. Normal right selective arteriogram.

II. ISOTOPIC RENOGRAPHY

The radioactive isotopic renogram simultaneously records the radioactivity over each kidney as I^{131} labeled orthoiodohippuric acid (hippuran) is cleared from the plasma and excreted into the urine. The normal curve consists of (1) an initial steep ascending limb as the hippuran bolus perfuses the renal vasculature, (2) a more gradual, progressive rise marking tubular accumulation and (3) a prolonged decline or excretion phase.[55,56] Analysis of the individual components of the curve by a number of investigators indicates that this separation into 3 well-defined functional segments represents a spurious oversimplification.[13,49,54] In addition, various extrarenal factors (accurate probe placement, immobilization of the patient, the state of hydration, salt depletion) as well as renal morphologic factors (shape and size of renal pelvis) influence the configuration of the curve.

A variety of comparative measurements has been proposed for the detection of unilateral abnormalities in renal function, *i.e.*, the steepness of the ascending limb of the curve, the relative height of the peaks, the interval from the time of injection to the peak count rate (T max.), the time from the point of the maximal count rate to the point of half of the latter value (T½) and a value based upon calculation of the percentage difference of retention of the isotope by each kidney.[13,49,55] The latter two determinations, which reflect the reduced urinary flow rate in the abnormal kidney, have proven to be the most reliable indicators of unilateral renal hypertension.

Although some clinics successfully perform isotopic renography in the sitting position, our results were not consistently reproducible. this way, probably due to inaccurate probe localization and difficulty in completely immobilizing the patient. Consequently, we constructed a simple plywood table with a lucite insert in the table top which facilitates roentgenographic localization of the kidneys and accurate placement of the probes under the table with the patient supine. The lucite window has a series of metallic shot 2.5 cm. apart embedded in the form of a cross in its center. With the patient lying supine on the table, a non-Bucky roentgenogram of the renal area is made, using a portable roentgenographic unit, and a cassette held in place in a tray beneath the lucite insert. The center of each kidney is marked on the developed film and the collimated scintillation detectors are correspondingly placed under the lucite window perpendicular to the patient's back, accurately centered on each kidney. After the examination, the cross on the roentgenogram is superimposed on the cross in the lucite window and the actual position of each detector is marked on the film as a permanent record. Hippuran (1.0 μc/kg.) is injected rapidly intravenously and the tracing continued for 30 minutes or until a baseline is reached. The percentage retention for each kidney at 10 and 20 minutes after the maximal count rate is calculated, using the peak value of each kidney as 100 per cent (Fig. 10, *A* and *B*). If both kidneys do not peak simultaneously, the earliest maximum count rate is used for calculating 10 and 20 minute retentions. A difference of more than 20 per cent retention between the two sides at any one time interval is indicative of vascular disease on the side with the slower fall-off, in the absence of urinary tract obstruction. Calculation of the fall-off rate of each kidney in terms of its own maximal count rate minimizes differences in peaks of the curves due to poor probe placement.

The demonstration either of an abnormal modified intravenous pyelogram or isotopic renogram suggesting renal vascular disease merits further study by aortography. In the authors' opinion, probably 90 per cent of patients with renal vascular hypertension can be detected by this screening procedure. Aortography is also offered to young patients with severe hypertension without an obvious cause even though the intravenous pyelogram and renogram are normal. This is done because of the dismal

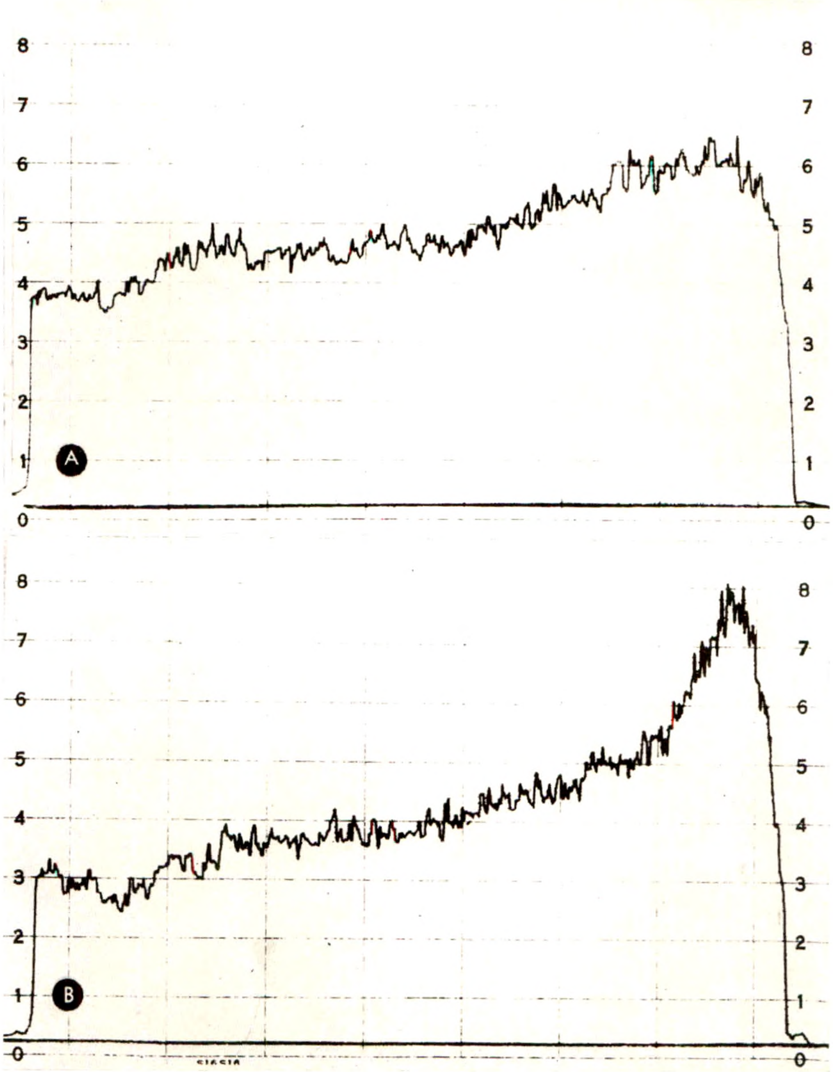

Fig. 10. (*A* and *B*) Isotopic hippuran renograms with a normal curve on the right side. The abnormal left kidney exhibits a lower initial peak and increased retention (right = 41 per cent and left = 69 per cent at 20 min.).

prognosis facing such patients unless an operable lesion is found.

III. AORTOGRAPHY

Some form of aortography is ultimately necessary to demonstrate the presence, site and character of the stenosis. We believe that the percutaneous femoral catheter technique is superior to translumbar aortography because it produces better renal arterial detail due to pump injection of the contrast medium, elimination of streaming resulting from poor placement of the needle and an opportunity for oblique views.[14,25,27]

We begin with an intra-aortic injection of 35 ml. of contrast medium through a teflon or polyethylene (PE 205) catheter containing several side holes and a suitably curved tip (for later use in selective renal arteriography). The injection is made at the end of deep inspiration using a Gidlund pump (or its equivalent) at a pressure of 6 kg./cm.^{2} with the tip of the catheter at the level of L2. The end hole of the catheter is occluded by a small round silver bead attached to a long stainless steel wire which is passed through the sidearm of a special stop cock.[38] Serial roentgenograms in the anteroposterior projection are made with a Schönander or similar apparatus and processed. The intra-aortic injection not only demonstrates the multiple renal arteries which are found in 20 to 30 per cent of patients but also provides an undistorted baseline study of the renal arteries (*vide infra*).

While these films are being processed, the tip-occluding wire is removed and the catheter is advanced under fluoroscopic guidance into one renal artery. A test injection of 2 ml. of contrast medium is made with a hand syringe under fluoroscopic control. If satisfactory, the catheter is pulled back slightly to avoid wedging and to decrease the possibility of spasm. Ten milliliters of contrast medium are injected by pump at a pressure of 3 kg./cm.^{2} and serial exposures are made in a slightly oblique projection with the kidney under study elevated 15 degrees, using a small focal spot (1.0 mm.) and careful coning. While the selective renal arteriographic films are being processed, the aortographic films are inspected. The selective renal arteriographic and aortographic films are then reviewed together. If there is a discrepancy in the appearance of the renal artery on the two studies or a more oblique projection seems advisable, a second selective injection and appropriate exposures are made. If the selective study is satisfactory, the catheter is withdrawn from the renal artery into the aorta, rotated and inserted into the contralateral renal artery under fluoroscopic control. After a test injection to confirm the position of the catheter, selective arteriography is carried out as it was on the first side.

This order is followed because we have encountered artifactual narrowing of the renal artery at or near the tip of the catheter during selective renal arteriography. We believe that the narrowing was due to spasm produced by the tip of the catheter or the jet since it was not present on the films exposed with the catheter in the aorta (Fig. 11, 12 and 13). Markland[31] has recently demonstrated the efficacy of papaverine in relieving renal artery spasm and we plan to use this drug in the future in problem cases. The selective arteriogram is important because it provides more detailed visualization of the segmental and intrarenal arterial branches than is possible with any intra-aortic injection, thus enhancing the possibility of detecting lesions in these vessels (Fig. 14 and 15).[36] Therefore, we consider the intra-aortic and the selective studies to be complementary rather than exclusive.

Originally, during the course of selective renal arteriography, we attempted to measure the pressure gradient across the area of narrowing when a stenotic lesion was demonstrated in a main renal artery.[2] This was done because of the clinical experience of many investigators indi-

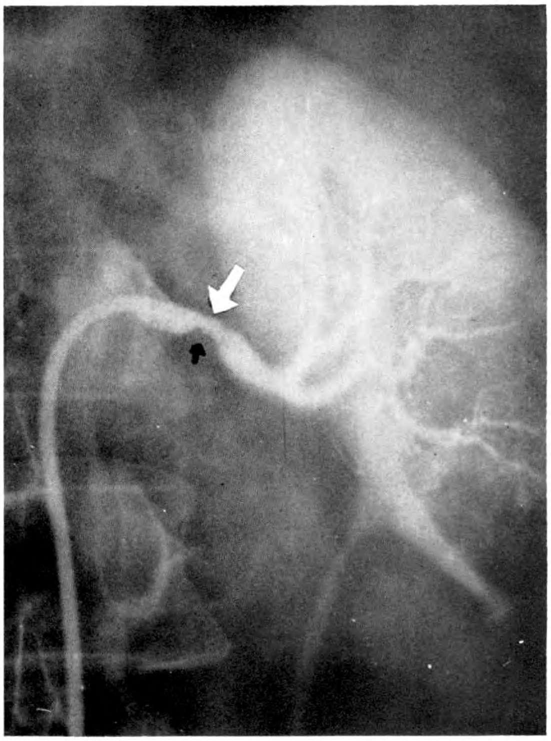

FIG. 11. Case v. Selective left renal arteriogram after the injection of 8 cc. of 76 per cent renografin into the superior of two renal arteries. Note the narrowing at the catheter tip.

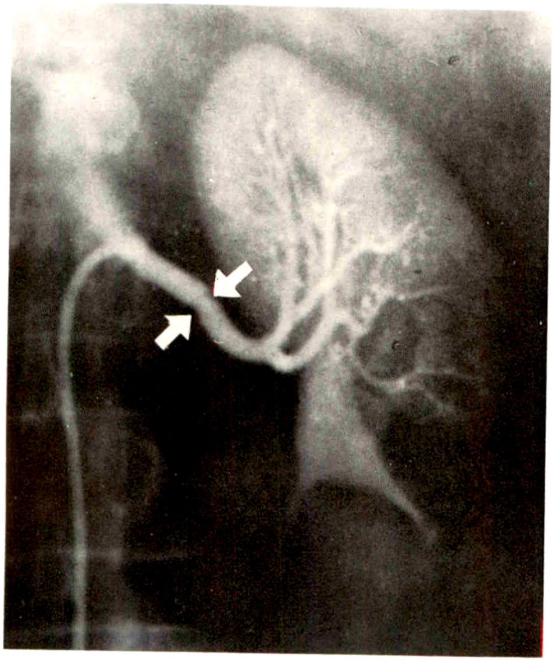

Fig. 12. Case v. Repeat selective left renal arteriogram 10 minutes after Figure 11 showing a decrease in the narrowing.

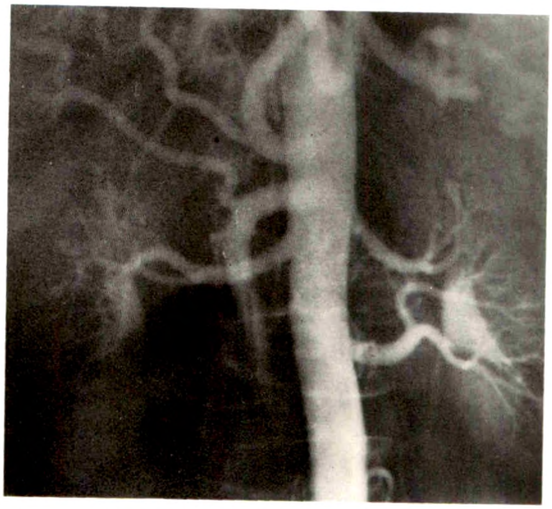

Fig. 14. Case v. Retrograde femoral aortogram using 40 cc. of 76 per cent renografin at a pressure of 6 kg./cm.² (Gidlund pump).

cating that patients with small gradients had little improvement of their hypertension following surgery. In this connection, Stewart *et al.*[48] reported that 89 per cent of a group of 17 hypertensive patients with a mean pressure gradient in excess of 40 mm. Hg had satisfactory relief of their hypertension following appropriate surgical treatment. Conversely, patients with a mean gradient of 10 mm. Hg or less were not significantly improved.

At present, we do not measure pressure gradients because experimental evidence suggests that abnormalities in renal function are a more sensitive index of functionally significant renal arterial stenosis than

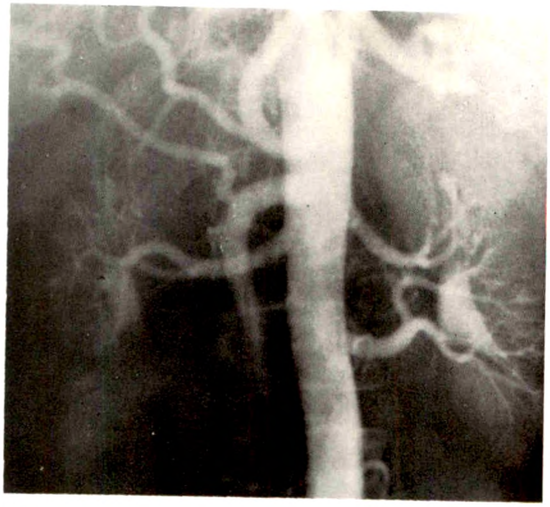

Fig. 13. Case v. Retrograde femoral aortogram made 30 minutes after Figure 11 demonstrating two normal renal arteries on the left side.

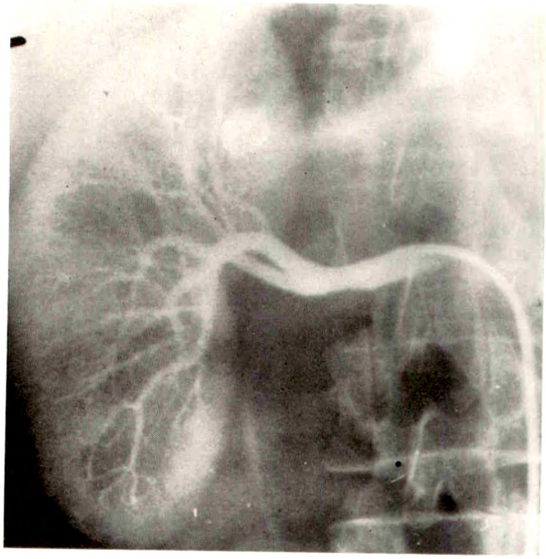

Fig. 15. Case v. Selective right renal arteriogram with 10 cc. of 76 per cent renografin and a pressure of 3 kg./cm.². Note the superior detail of the intrarenal arterial tree.

manometric studies. Thus, Maier *et al.*[30] have shown that no functional changes or pressure gradient are detectable in dogs in whom the stenosis is less than 40 per cent of the renal arterial diameter (60 per cent cross-section area reduction). Moreover, a decrease in renal function, *i.e.*, reduction in glomerular filtration rate, renal plasma flow, urine flow and urine sodium excretion constantly occurs before the critical stenosing zone for manometric changes is reached, *i.e.*, above 60 per cent of the renal arterial diameter (84 per cent cross-section area reduction).

IV. RENAL SPLIT FUNCTION STUDIES

We believe that patients with renal arterial stenosis demonstrated by aortography should receive renal split function studies.[6,10,22] This can be done by evaluating the concentration of inulin and paraminohippurate (PAH) after infusion, as Stamey *et al.*[47] have recommended or by substituting determinations of creatinine and urea concentrations. Since the determination of inulin and PAH concentration is not a routine laboratory procedure in most hospitals, the concentration of urea or creatinine in the urine may provide a more universally available method of satisfactory accuracy.[49] We also believe that patients with an abnormal intravenous pyelogram and isotopic renogram but normal aortogram should be examined by this technique because of the possibility of multiple focal peripheral arterial lesions.

In Howard and Connor's[23] experience, patients with stenosis of one *main* renal artery whose hypertension had been cured by surgery consistently exhibited the following functional abnormalities in the urine of the diseased kidney: (1) a reduction in volume of 60 per cent or more; (2) a reduction in sodium of 15 per cent or more; and (3) an increase in creatinine of 50 to 100 per cent. We consider such patients to be candidates for surgical therapy.

However, the findings are by no means so clear cut in segmental disease due either to obstruction of one or more renal artery branches (usually detectable by selective arteriography) or to more peripheral diffuse patchy involvement. The variable functional pattern under these circumstances is understandable since the ischemic segment, if severely involved, may secrete no urine or if less severely involved, may secrete urine with varying degrees of reduced volume and sodium content. Howard and Connor[23] have reported the following nonspecific spectrum of functional abnormalities in the urine of the diseased kidney with segmental vascular involvement:

(1) a reduction in volume, usually of the order of 33 to 50 per cent; (2) an inconstant reduction in sodium concentration of the order of 20 per cent; however, the sodium concentration may be equal or even greater than the normal side; and (3) an increase in creatinine of the order of 20 to 30 per cent.

The nonspecificity of these findings is troublesome, particularly in the absence of a demonstrable arteriographic lesion, when one recalls that some patients with essential hypertension have presented similar functional changes. Further problems in the interpretation of the differential renal split function test may arise in patients with bilateral renal artery stenosis. In both of these situations, *i.e.*, in suspected segmental involvement or bilateral renal artery stenosis with atypical split function tests, we believe that further investigation is indicated by renal biopsy and bioassay of pressor substances.

V. BIOASSAY OF PRESSOR SUBSTANCES AND RENAL BIOPSY

Helmer[20] has devised a relatively simple bioassay method for the determination of vasoconstrictor substances in the renal vein blood of hypertensive patients. Heparinized samples of blood from each renal vein are obtained by percutaneous transfemoral catheterization and dialyzed to separate the insoluble protein fraction. The dialysis removes the water soluble pressor substances such as the catecholamines and serotonin while the proteins, renin, renin substrate and angiotensin do not dialyze out. The plasma is added to a chamber containing a spirally-cut rabbit aortic strip bathed in a Krebs-bicarbonate-glucose solution. The vasoconstrictor response is recorded by a heart lever, one end of which is attached to the aortic strip and the other to a writing instrument. Renal vein plasma from the abnormal kidney produces a strong contraction, while that from the normal kidney has the same activity as the control, *i.e.*, brachial vein blood.

During selective renal vein catheterization to collect blood for bioassay, it is easy to perform renal vein clearance studies as suggested by Abrams and his co-workers.[1] According to these investigators, the renal vein draining a normal kidney is cleared of radiopaque contrast medium within 3 seconds while the vein on the abnormal side has a delayed clearance time (Fig. 16; and 17, *A*, *B*, *C* and *D*).

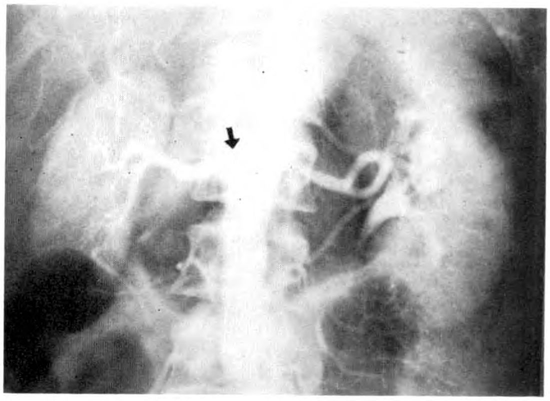

Fig. 16. Case vi. Retrograde femoral aortogram showing stenosis of the right renal artery close to its origin.

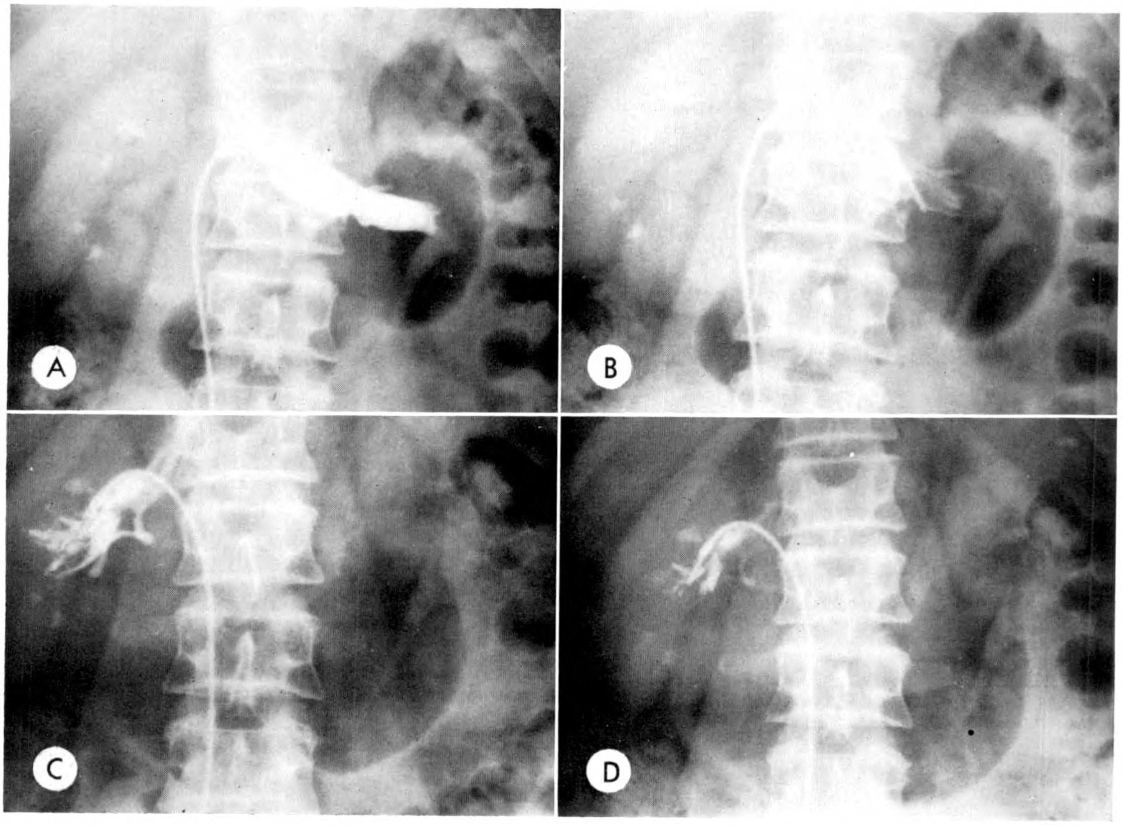

Fig. 17. Case vi. Selective catheterization of both renal veins. (*A*) Injection of 50 per cent hypaque into the left renal vein. (*B*) Prompt clearing of the contrast medium from the left renal vein within 2 seconds. (*C*) Injection of 50 per cent hypaque into the right renal vein. (*D*) Persistence of contrast medium in the right renal vein at 4 seconds.

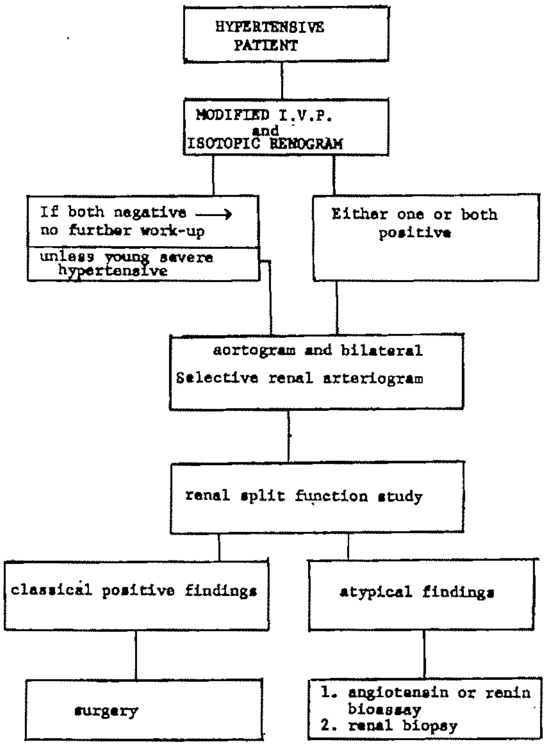
HYPERTENSIVE PATIENT
MODIFIED I.V.P. and ISOTOPIC RENOGRAM
If both negative ⟶ no further work-up
unless young severe hypertensive
Either one or both positive
aortogram and bilateral Selective renal arteriogram
renal split function study
classical positive findings
atypical findings
surgery
1. angiotensin or renin bioassay
2. renal biopsy

FIG. 18. Schema for work-up of a patient suspected of having renal hypertension.

Although our own personal experience with this test is limited and we have not carried it out with the elegance of the Stanford group, we have not found it to be the decisive factor in resolving the problem case.

It is well known that diffuse intrarenal arteriolar sclerosis can produce hemodynamic and functional changes identical to those resulting from stenosis of the main renal artery. These lesions are commonly bilateral and not necessarily symmetrically progressive in both kidneys. Hence, patients with atypical split function tests who lack arteriographic evidence of a stenotic lesion can benefit from bilateral renal biopsy.[51,58] If biopsy of the kidney thought to be normal on the basis of the split function tests demonstrates normal findings or minimal vascular disease, a functionally significant, surgically remediable process exists in the opposite kidney. If, on the other hand, biopsy reveals severe bilateral arteriolar sclerosis, the lesion is not amenable to surgical correction.

SUMMARY

1. The authors have presented a review of the currently accepted hypothesis of the etiology of renal vascular hypertension, and the pathophysiologic characteristics of the involved kidney.

2. Figure 18 shows a logical plan for studying the patient suspected of having renal vascular hypertension.

3. A modified technique of intravenous pyelography, the role of isotopic renography, angiography, renal split-function tests, bioassay of pressor substances and renal biopsy in this connection are discussed.

4. The advantages, disadvantages and problems involved in various types of renal angiography are considered.

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ANGIOMYOLIPOMA OF THE KIDNEY

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BENIGN renal tumors of clinical importance are extremely rare. Small lesions which remain undiscovered until autopsy are somewhat more common, but Foster,[6] reviewing the literature in 1956, was able to find only 135 benign renal growths of sufficient size to produce symptoms and be discovered during life. Of these, 24 were diagnosed histologically as lipomata and 8 others were considered mixed tumors.

Clinically, the hamartomata or mixed tumors appear to occur in two general forms. There are the small lesions which are frequently multiple, often bilateral and usually asymptomatic. These are more often seen in younger individuals and Moolten[14] has shown that they are a frequent accompaniment of tuberous sclerosis. It has been pointed out that renal tumors are present in 80 per cent of cases of tuberous sclerosis, but these are asymptomatic and rarely diagnosed before autopsy.[8] Because of this common association and the occurrence of hamartomatous lessions elsewhere in the body in tuberous sclerosis, the term disseminated hamartosis has sometimes been employed for the entity.

However, it is not this form of hamartoma with which we are concerned, but rather the larger tumors. These are solitary, in general, although additional smaller foci may be present. They are not associated with tuberous sclerosis, occur in an older age group (fourth to sixth decades, in particular) and show a definite predilection for females. Usually, they become symptomatic because of their size alone, although occasionally there may be hemorrhage producing pain. Hematuria, however, is uncommon.

While the proportions of the different tissues present are highly variable, fat is generally predominant, particularly in the center of the lesion.[2] The renal parenchyma has no genuine adipose tissue and it is considered that the lipomatous elements are derived from the renal capsule, although the origin is admittedly an involved one. Usually, muscular and vascular elements are also found, the former derived from the blood vessels. Because of the combination of these three tissues, the term angiomyolipoma has been considered the best histologic appellation. Etiologically, the tumors are considered most likely congenital errors or malformations.[3] Other theories such as true neoplasia or lipomatous metaplasia seem less tenable.

It is important to differentiate these growths from extrarenal retroperitoneal lipomata since the former almost never become malignant. Each of 2 cases reported by Edelman[4] in 1951 as renal liposarcomata had long survivals and subsequent histologic review[10] has established that these were undoubtedly benign.

DIAGNOSIS

Angiomyolipomas have practically never been diagnosed accurately preoperatively since the roentgenographic findings are rarely pathognomonic. Some authors[9,10,21] have pointed out that the high fat content of the tumor may cause areas of radiolucency to be seen within the mass. However, because the fat is usually scattered throughout the lesion, this may not be readily apparent on roentgenograms.

Khilnani and Wolf,[10] in one of the very few articles devoted to the roentgenographic diagnosis of renal hamartomata, placed the roentgen findings into two groups: (1) signs indicative of a mass (and thus nonspecific); and (2) signs suggesting the presence of fatty tissue within the mass. They felt that the lucent areas were usually non-demarcated, nondescript and

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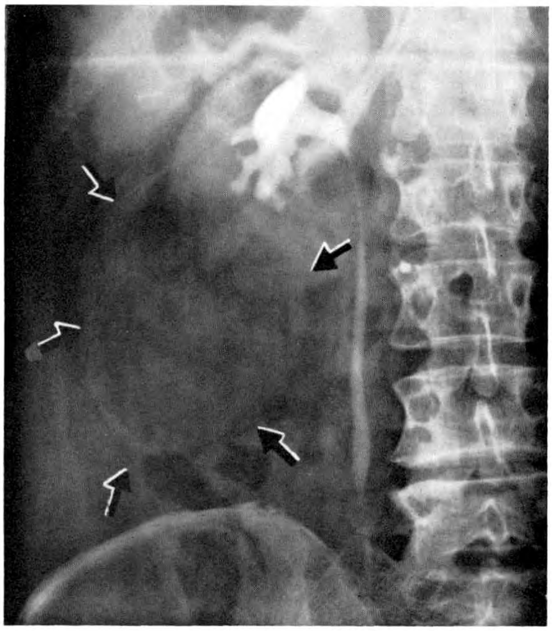

FIG. 1. The large mass lesion arising from the inferior pole of the right kidney is clearly seen. There appears to be a distinct, relatively thick, capsule surrounding the mass with a definite, almost homogeneous, radiolucency within it. The rotation of the kidney about its horizontal axis and the slight distortion of the lower pole calyces due to crowding are also demonstrated.

irregular and required careful search to be seen.

In our case, the distribution of fat in the tumor was such that we were able to realize immediately that we were dealing with a large fat-containing tumor of the kidney, and the correct diagnosis was suggested preoperatively. For these reasons, this case is deemed worthy of report.

REPORT OF A CASE

F.B., a 57 year old white female, was admitted to Oxford Hospital on the service of Dr. Joseph Levin on September 29, 1964. She complained of pain on the right side of the abdomen which had been present intermittently for about 1 week prior to admission. There had been a 5 pound weight loss in the previous 2 weeks, but otherwise the patient had been well and asymptomatic. She had undergone a hysterectomy at the age of 27, but the past medical history was otherwise noncontributory. System review was negative except for nocturia.

Physical examination revealed a normally developed and nourished individual in no distress. The blood pressure was not elevated. Physical findings were limited to the abdomen which was soft but slightly tender in the right flank. A somewhat rounded, barely movable, slightly tender mass was felt here. There was mild left costovertebral angle tenderness. The impression was: "abdominal mass, probably renal tumor, retroperitoneal sarcoma, lymphoma or neurofibroma." Laboratory studies were completely negative; urinalysis was normal with no microscopic hematuria. The blood urea nitrogen was 9.6 mg. per cent.

Intravenous urography was performed on September 30, 1964. A large mass, approximately 7×9 cm. arising from the inferior pole of the right kidney, was demonstrated (Fig. 1). The kidney itself was rotated around its horizontal axis and there were slight pressure changes in the lower pole calyces, but no intrinsic abnormality of the collecting system itself was noted. The mass appeared to have a capsule, several millimeters thick, while the central portion was rather homogeneously lucent. Because of this appearance, a high fat content was postulated and it was felt that we were dealing with a lipoma or hamartoma.

Surgical intervention (Drs. Lester Karafin and Richard Kendall) on October 1, 1964 revealed a neoplasm involving the lower pole of the right kidney, presenting anteriorly. By palpation, the lesion was considered to be somewhat cystic but the wall seemed thickened, hemorrhagic and fatty. Needle aspiration was attempted but yielded only blood. The kidney was then removed. The kidney itself appeared quite small with the tumor representing the entire lower and middle poles. The surgical impression was a hamartoma with lipomatous and angiomatous elements.

According to the pathologic report (Dr. Harvey Watts), the specimen was a kidney of approximately normal size. At one pole there was a rounded tumor mass, 7.5 cm. in diameter. It appeared to be encapsulated, although the capsule had been ruptured. Its substance was soft, firm and generally yellow tissue, grossly resembling adipose tissue. Some areas showed fresh hemorrhage, and there were firmer grayish-white portions, especially in the area adjacent to the renal tissue. Within the kidney itself, there were two similar nodules, one in the medulla and one at the corticomedullary junction area, both measuring 1.2 cm. in diameter.

There was no evidence of involvement of the pelvic tissues or of the vascular pedicle.

Sections revealed a mixture of smooth muscle cells, small arterial type and venous blood vessels with prominent muscular coats, and adult type adipose tissue, the latter making up the bulk of the lesion. This combination of tissues is peculiar to a lesion of generally benign prognosis, an angiomyolipoma. These lesions arise in or from the renal substance or from the renal capsular tissue. They are generally considered to be hamartomatous in nature. Because the lesion in this case apparently had had its capsule ruptured, some of it might have been left in the patient. Except for the possibility of a recurrence, it was felt that a benign course could be expected. The smaller lesions within the kidney showed a similar appearance, and it was, therefore, judged that the lesion was multifocal.

The pathologic diagnosis was angiomyolipoma of the kidney.

The patient experienced an uncomplicated postoperative course and was discharged in excellent condition on October 11, 1964.

CONCLUSIONS

Hamartomatous lesions of the kidney, large enough to cause symptomatology, are extremely rare tumors and are practically never diagnosed as such preoperatively. A case is reported in which the distribution of fat throughout the mass rendered an appearance considered sufficiently typical to allow a correct preoperative diagnosis to be suggested.

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ANGIOGRAPHIC FEATURES OF ANGIOMYOLIPOMA OF THE KIDNEY

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RENAL angiomyolipoma is a form of hamartoma; hamartoma being defined as an abnormal development of mature tissue natural to the site or organ, representing a non-neoplastic growth.[4]

Renal hamartomas are of two varieties: (1) medullary fibromas and (2) hamartomas of mixed mesenchymal origin. The latter type are usually small multiple lesions found at autopsy in patients with tuberous sclerosis. The rare angiomyolipoma found in the absence of tuberous sclerosis is characteristically unifocal and may become very large, and occurs most often in females in the third to fifth decade of life.[3] There is dispute as to whether these tumors ever undergo malignant degeneration. Most previous reports state that the so-called malignant angiomyolipomas are really malignant mesenchymomas from their inception.[1,2]

Presentation of symptoms by the patient is rare; the condition is usually discovered coincidentally during physical examination by the finding of a slow-growing, palpable abdominal mass. Occasionally, however, a patient complains of flank pain; this is not usually accompanied by hematuria because hemorrhage is into the tumor mass and is not associated with extension into, but rather compression of, the renal parenchyma. One other occasional complaint is fever.

Preoperative diagnosis has always been difficult in the patient without tuberous sclerosis. The only clue to the presence of a hamartoma, as opposed to a malignant lesion in a patient demonstrating any of the above symptoms, is a slowly growing mass and the radiolucent appearance on roentgenograms of fat tissue overlying the mass.[9]

To this date, there have been only 29 cases reported in the English literature of renal angiomyolipomas unassociated with tuberous sclerosis. Four of these have had angiographic studies of the kidney by

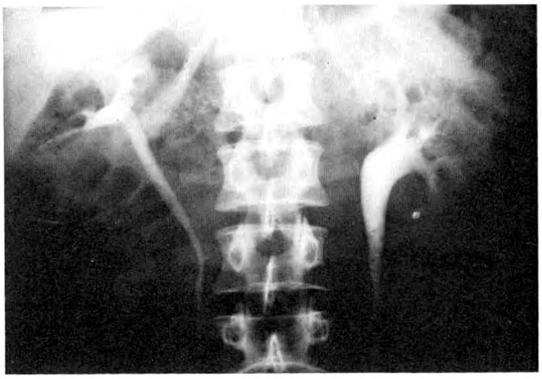

FIG. 1. Intravenous pyelogram showing a right lower pole mass compressing the calyces and displacing the proximal ureter medially.

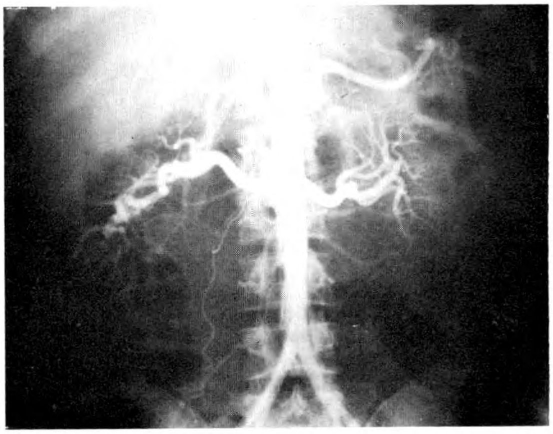

FIG. 2. Three-quarter second angiogram. The right renal artery is seen to be larger than the left. There is immediate visualization of abnormal tumor vessels which are somewhat coarser in character than those usually seen in hypernephroma.

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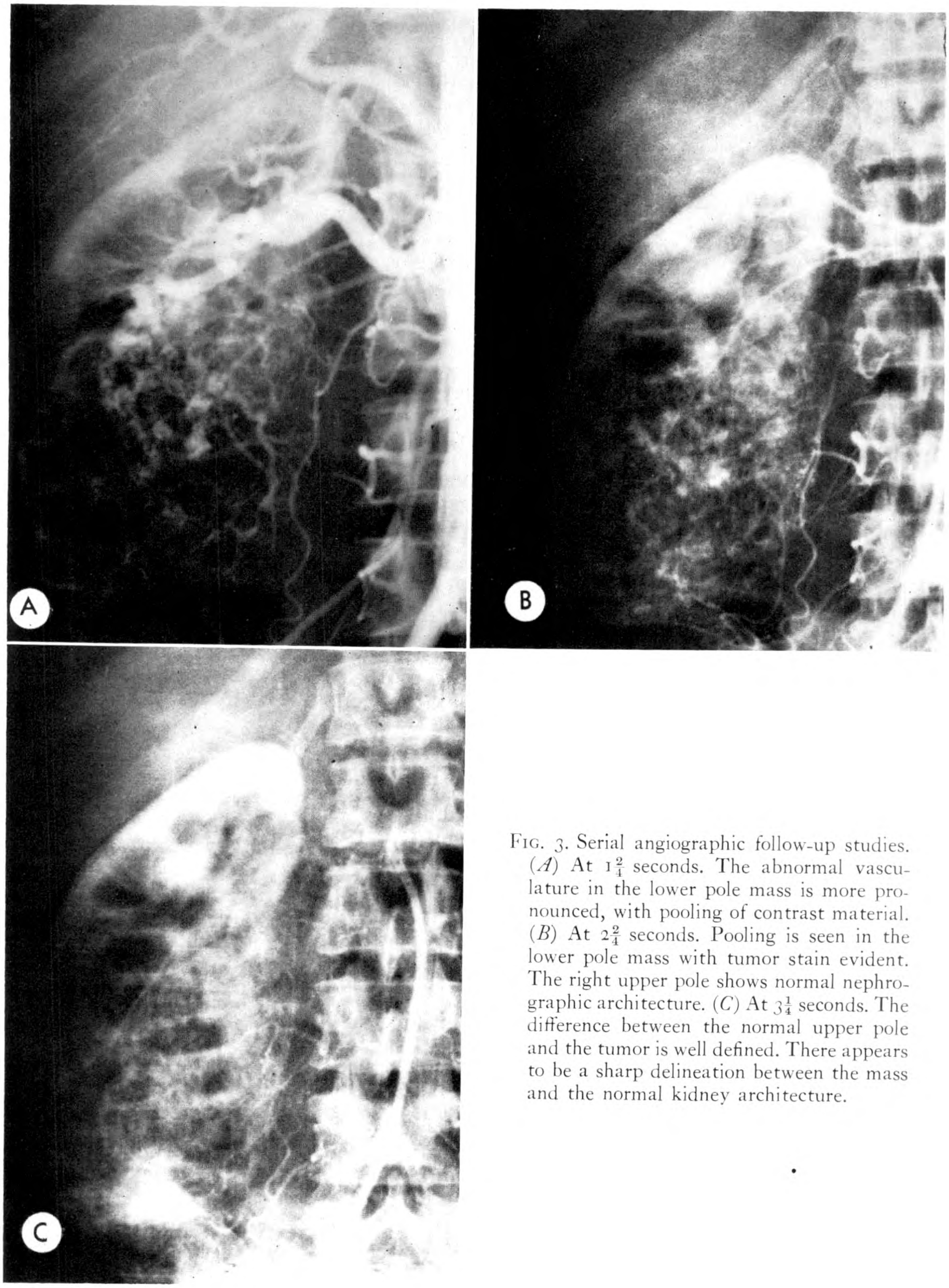

Fig. 3. Serial angiographic follow-up studies. (*A*) At $1\frac{2}{4}$ seconds. The abnormal vasculature in the lower pole mass is more pronounced, with pooling of contrast material. (*B*) At $2\frac{2}{4}$ seconds. Pooling is seen in the lower pole mass with tumor stain evident. The right upper pole shows normal nephrographic architecture. (*C*) At $3\frac{1}{4}$ seconds. The difference between the normal upper pole and the tumor is well defined. There appears to be a sharp delineation between the mass and the normal kidney architecture.

translumbar aortography.[4,5,7,8] Our case has had a serial angiographic study by means of the Seldinger technique.

REPORT OF A CASE

A 32 year old Puerto Rican female was first seen at Cook County Hospital on October 29, 1964, complaining of vague right upper quadrant abdominal pain, intermittently present for 3 years. She claimed to have had one episode of dark urine, but the actual presence of gross or microscopic hematuria could not be documented. She had been anorexic and lost 15 to 20 pounds in the previous 6 months. Three years prior to admission, she was told by another physician that she had an "enlarged" right kidney, and surgery was advised at that time.

Physical findings were limited to a hard, tender, right upper quadrant abdominal mass, extending from the costal margin to the umbilicus. There were no signs of tuberous sclerosis, and she was afebrile.

Intravenous pyelograms on November 1, 1964 (Fig. 1) showed displacement of the right renal collecting system upwards, with flattening and elongation of the right lower pole calyces by a mass; there was no evidence of invasion of the calyceal system.

On November 5, 1964, renal angiography was performed by the Seldinger technique.[6] With the tip of the catheter at the level of the interspace between the first two lumbar vertebrae, 50 cc. of conray 400 was injected with serial filming in the anteroposterior projection. The findings were compatible with a tumor in the lower pole of the right kidney, which was thought to be a hypernephroma (Fig. 2; and 3, *A–C*).

At surgery on November 10, 1964, a grapefruit-size mass was found in the lower pole of the right kidney, and a right nephrectomy was performed.

PATHOLOGIC FINDINGS

The specimen consisted of a 450 gm. kidney with the tumor mass, measuring 8.5×8.0×6.0 cm., replacing the lower pole. The cut surface was pinkish with several yellow foci. The mass was well delineated from the surrounding renal parenchyma.

Microscopic examination revealed the tumor to consist of smooth muscle bundles which appeared to arise from the walls of vascular channels and which were intermingled with foci of fat tissue. The diagnosis was angiomyolipoma (Dr. Paul Szanto).

SUMMARY

Angiomyolipoma of the kidney is usually a benign tumor which is frequently associated with tuberous sclerosis. Renal angiographic studies demonstrate vascular patterns reminiscent of malignant tumor.

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POSITION OF THE KIDNEYS RELATIVE TO THE SPINE, WITH EMPHASIS ON CHILDREN*

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PREVIOUS INVESTIGATIONS IN ADULTS

HELM[5] evaluated the position of the kidneys in 104 postmortem examinations: 70 males and 34 females, 92 adults and 12 children. He found that the right kidney was lower than the left in two-thirds of the cases, and that in males the kidneys were approximately one-half of the height of a vertebral body higher than in the females. In most cases, the upper pole of the kidney was at the level of T11–T12, while the level of the lower pole varied from the top of L3 to the L3–L4 interspace.

Büdinger[2] studied 60 random autopsies, practically all in adult individuals. In most cases the upper poles were at the level of T11–T12 and the lower poles were opposite L2–L3.

Moody and Van Nuys[8] studied roentgenographically 225 "normal" young males and 225 "normal" young females. In the males the upper and lower poles on the right were at the level of T12–L1, and L3–L4, respectively, while the upper and lower poles on the left were at the level of T11–T12 and L2–L3, respectively. In the females, the corresponding levels on the right were T12–L1, and L3–L4, and those on the left were T11–T12 and L2–L3.

McClellan[6] reviewed 1,500 consecutive excretory urograms, and found that the left kidney was "normally" lower than the right in 5.1 per cent of the cases.

Edsman[4] evaluated roentgenographically the position of 245 right and 222 left kidneys of living subjects, apparently all adults. All the roentgenograms were made in expiration. He found that the center of the right kidney, on the average, was 0.2 unit cranial to the upper third of L2 and the left kidney was 0.5 unit caudal to the lower third of L1, one unit being equal to one-third of the height of a vertebral body.

Anson and Daseler[1] investigated at postmortem examination 193 right and 194 left kidneys. The upper and lower poles of the right kidneys were respectively at the level of T12–L1 and L3–L4, while the corresponding levels on the left were T12–L1, and L3.

Möell[7] studied roentgenographically 100 "normal" adult males and 100 "normal" adult females. In the males the upper pole on the right was 6.9 cm. ($1\sigma = 1.69$) above and the lower pole was 5.2 cm. ($1\sigma = 1.83$) below, respectively, the center of L2; on the left the corresponding figures were 8.4 ($1\sigma = 1.51$) and 4.2 ($1\sigma = 1.51$) cm., respectively. In females, the upper pole on the right was 6.3 cm. ($1\sigma = 2.05$) below and 5.5 cm. ($1\sigma = 1.97$) above the center of L2; on the left the corresponding figures were 8.1 ($1\sigma = 1.45$) and 4.1 cm. ($1\sigma = 1.49$).

PREVIOUS INVESTIGATIONS IN CHILDREN

The only investigation relative to the position of the kidneys in children is that by Petrén,[10] but his work was not available to us for this review. In reference to this work, Olsson[9] states that "in children the kidneys are relatively lower than in adults and it is claimed (Petrén, 1934) on the basis of anatomic studies that the right kidney assumes its definitive position at the age of 5–7 years, the left at 8–10 years."

PRESENT INVESTIGATION IN CHILDREN

In an attempt to obtain some information on the level of the kidneys in children relative to the spine, we have reviewed the roentgenograms of 100 unselected children (50 males and 50 females) who had excre-

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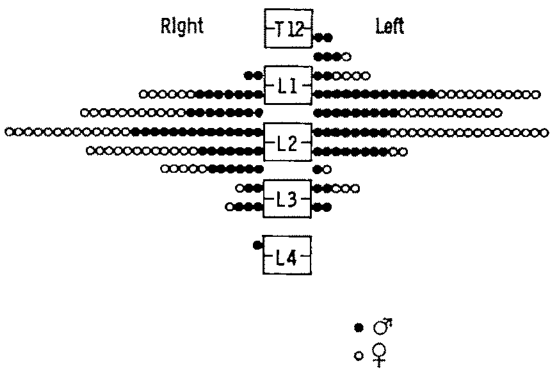

FIG. 1. Position of the center of the right and left renal pelvis relative to the spine in the 100 children included in this study.

tory urographies but no roentgen evidence of perirenal or upper urinary tract abnormality. Their ages at the time of urography ranged from 7 days to 14½ years. For convenience, the center of the renal pelvis was taken as the landmark. A line perpendicular to the spine was drawn from this point and the level on the corresponding vertebral body or intervertebral disk space was recorded. The vertebral bodies were divided into an upper and lower half.

The results of the study, summarized in Figures 1, 2 and 3 are as follows:

The position of the right renal pelvis in relation to the spine ranged widely, but its most common location (66 per cent of the cases) was between the L1–L2 interspace and the lower half of L2 (average: upper half of L2). The position of the left renal pelvis also ranged widely, but its most common location (69 per cent of the cases) was between the lower half of L1 and the upper half of L2 (average: L1–L2 interspace).

The right kidney was lower than the left in 61 per cent of the cases: the two kidneys were at the same level in 33 per cent; and the left kidney was lower than the right in 6 per cent (Fig. 2). These figures correspond closely to those reported in adults.

The position of the right renal pelvis had the same range and distribution relative to the spine in the patients in whom the right kidney was lower than the left, as well as in the patients in whom the two kidneys were at the same level or when the left was lower than the right (Fig. 2). These findings

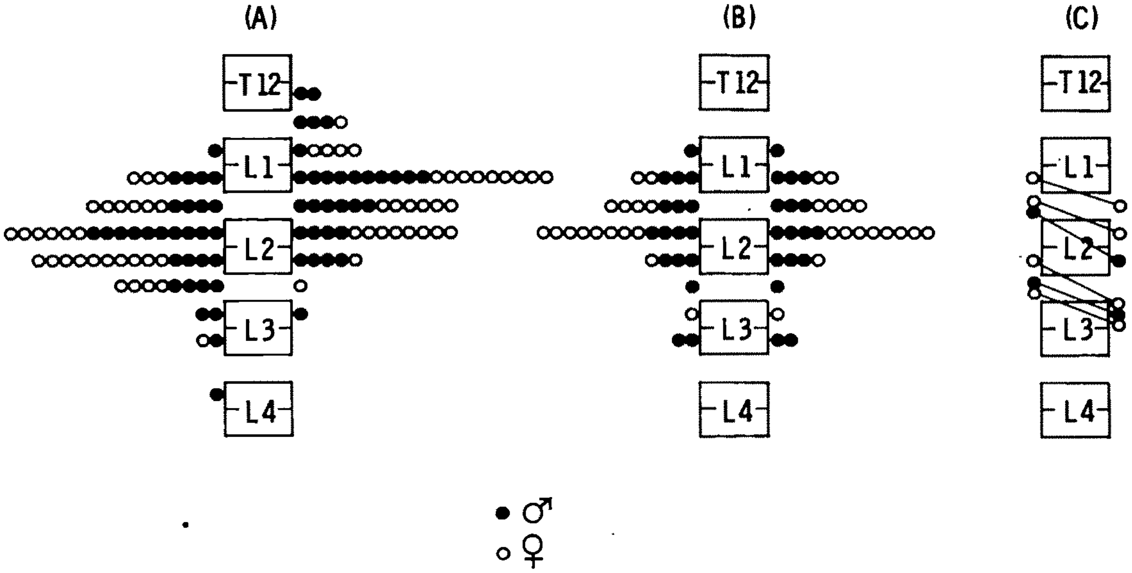

FIG. 2. Position of the center of the right and left renal pelvis relative to the spine: (A) in the 61 children (31 males and 30 females ranging in age from 7 days to 14½ years) in whom the right kidney was lower than the left; (B) in the 33 children (17 males and 16 females ranging in age from 1 month to 13 years) in whom the two kidneys were at the same level; and (C) in the 6 children (2 males and 4 females ranging in age from 1 month to 13 years) in whom the left kidney was lower than the right.

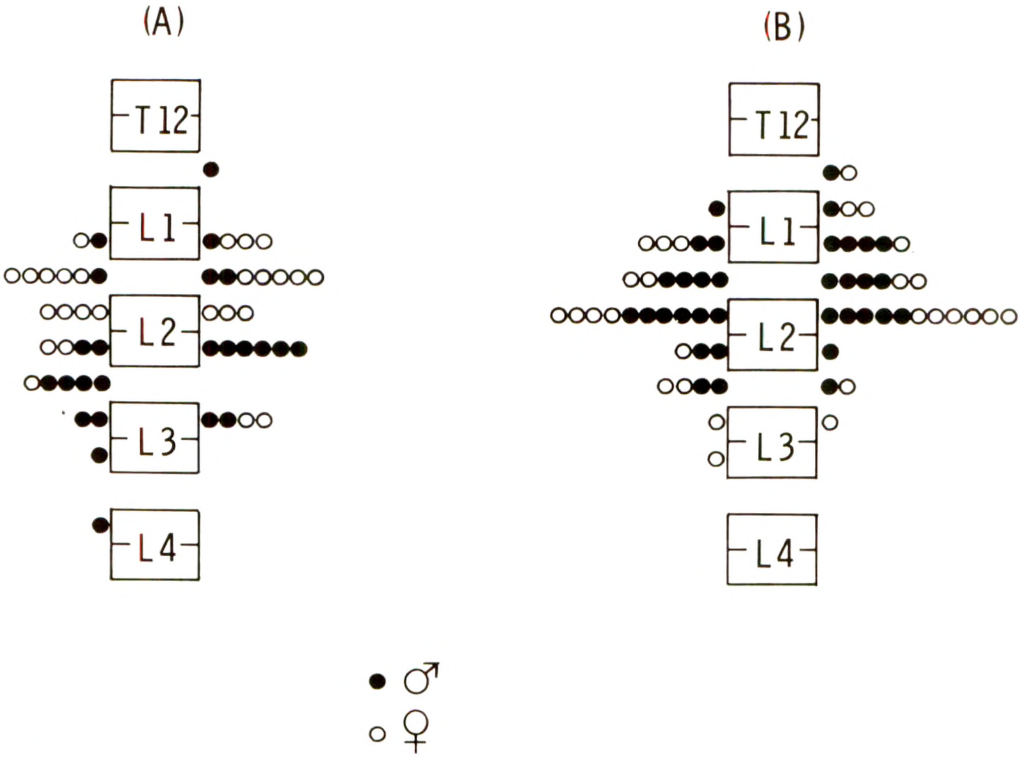

Fig. 3. Position of the center of the renal pelvis relative to the spine: (A) in the children of the series who were less than 1½ years of age, and (B) in the children who were older than 10 years.

suggest that the difference in the position of the kidneys on the two sides is mainly at the expense of the left kidney.

In 57, or 85 per cent, of the 67 patients in whom the two kidneys were not at the same level, the difference in height between the two kidneys relative to the spine was half the height of one vertebral body in 34 cases (16 males and 18 females), of one vertebral body in 23 cases (9 males and 14 females), of one and a half vertebral bodies in 9 cases (6 males and 3 females), and of two and a half vertebral bodies in one male.

Contrary to the findings obtained in some adult series, there was no definite difference in the position of either kidney between males and females. Also, there was no definite relation between the sex of the patient and the position of the kidneys relative to one another. As shown in Figure 3, there was no clear cut difference in the position of the kidneys between younger and older children, a finding which contradicts the results reportedly claimed by Petrén[10] that the kidneys ascend in the abdomen during childhood.

Finally, we have attempted to determine whether there was any definite difference in the position of the kidneys relative to the spine between children and adults. For this purpose, we have calculated the position of the renal pelvis in all the patients included in the adult series quoted above, and have compared the findings with those in our patients. The center of the pelvis in the reported adult series was calculated on the basis of the given renal length and the data furnished by Zondek[11] relative to this point; according to this author, the distance between the center of the renal pelvis and the border of the upper pole varies from 5.2 to 7.9 cm. (average 6.44 cm.) and the corresponding distance for the lower pole ranges from 4.1 to 6.2 cm. (average 4.98 cm.). In Edsman's[4] series, where only values for the center of the kidney were given, the approximate renal length was first estimated from the average measurements of normal kidneys reported in the literature.[3] The results of this comparison revealed that the renal pelvis in our series of children was essentially at the same level relative to the spine as in the adults, in whom the center of the renal pelvis, on the average, corresponded to the top part of L2 for the right kidney and to the L1–L2 interspace for the left kidney.

SUMMARY

In a series of 100 children from 7 days to 14½ years of age, it was found that in most cases the pelvis of the right kidney was at the level of L1–L2 (average L2), while the left pelvis lay in most cases between the lower half of L1 and the upper half of L2 (average: L1–L2 interspace). The right kidney was lower than the left in approximately two-thirds of the cases, the two kidneys were at the same level in one-third, and the left kidney was lower than the right in 6 per cent. When the two kidneys were not at the same level, the difference in their height relative to the spine usually was of one vertebral body or less, seldom more. The age and sex in childhood did not seem to influence significantly the position of the kidneys. Also, a review of data reported in adults showed no clear-cut evidence of any difference in location of the kidneys relative to the spine between children and adults.

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THE VALUE OF THE POSTANGIOGRAPHIC PYELOGRAM*

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THE purpose of the authors is to emphasize the significance of obtaining an abdominal roentgenogram after any procedure in which absorbable iodinated contrast material had been administered to a patient. The mode of administration of the radiopaque contrast medium may be by the intravascular, extravascular or alimentary route. The intravascular injection of radiopaque medium (by intravenous or intra-arterial means) is expected to produce a good to excellent pyelogram. A satisfactory examination of the urinary system may be obtained from the extravascular administration of contrast medium (by subcutaneous, intramuscular, sinus tract or intra-articular injection). The gastrointestinal route (by mouth or T-tube cholangiography) is expected to produce a poor pyelogram, but the urinary tract may be fairly well demonstrated when a sufficient amount of the iodinated material is absorbed into the blood stream.

Whatever modality is used to administer the absorbable radiopaque contrast material to the patient, the abdominal roentgenogram taken as a delayed film after the initial study is important. It is a gross roentgenologic gauge of renal function and anatomy (Fig. 1 through 8).

Since a good pyelogram is produced following intravascular injection of contrast material, a delayed abdominal roentgenogram, obtained in patients who have undergone angiography, can be most helpful. A review was made of the cases from the Cardiovascular Radiology Suite of the Yale-New Haven Medical Center (January, 1962 to December, 1964, inclusive) and the Department of Radiology, West Haven Veterans Administration Hospital (July, 1963 to June, 1964, inclusive) in which this procedure was used. The studies of the abdominal aorta and its branches were eliminated from the series since intravenous pyelography usually precedes the aortic examination. The incidence of urinary tract diseases detected on the postangiographic pyelogram is shown in Table 1. Unfortunately, the study was not obtained in several patients. We have recently instituted this additional examination in our neuroradiologic service. It is felt that it may be especially useful in patients with subarach-

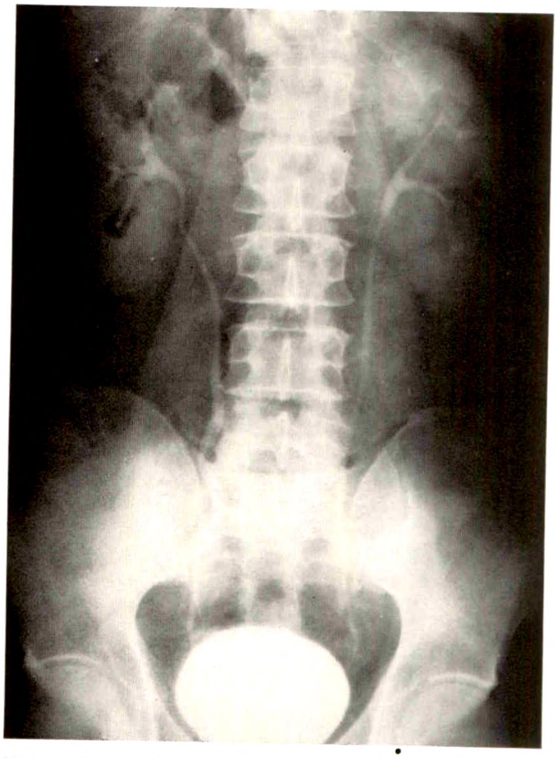

FIG. 1. Postangiographic pyelogram of a patient after pulmonary arteriography for a lung tumor. There is excellent visualization of the normal urinary tract.

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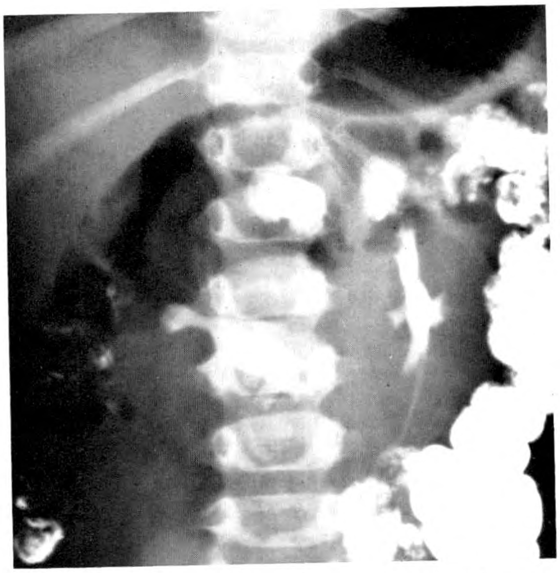

FIG. 2. Horseshoe kidneys are demonstrated in a patient who had undergone angiography for transposition of the great vessels with coarctation of the aorta.

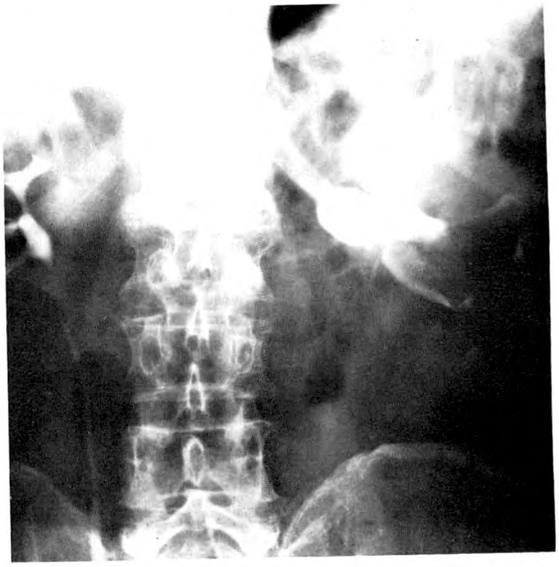

FIG. 4. The postangiographic pyelogram of a patient after venography for a superior vena cava syndrome due to a mass in the right chest and mediastinum. Unfortunately, postmortem examination was refused so that a definitive diagnosis of the mass in the left kidney was not made (primary or metastatic carcinoma?).

noid hemorrhage secondary to rupture of an intracranial aneurysm.[3]

The postangiographic pyelogram serves as a scout survey for urinary tract pathology. The congenital anomalies and the acquired diseases of the urinary tract detected by this method of examination are shown in Table II. For reasons already stated, these abnormalities represent the *minimal* number. The incidence of urinary tract pathol-

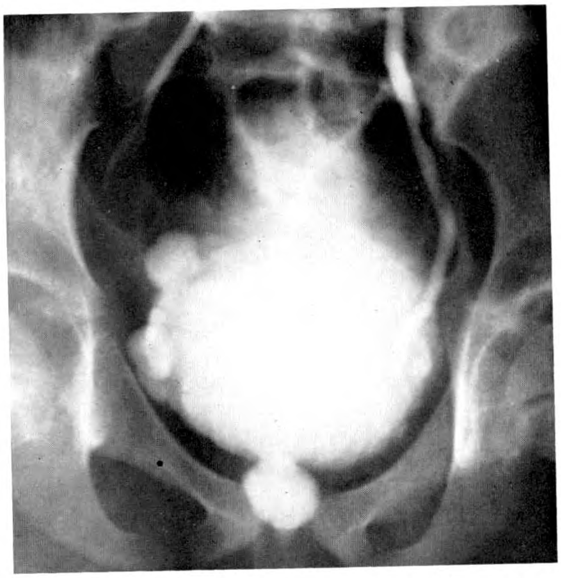

FIG. 3. Multiple vesical diverticula are shown in a patient with ventricular septal defect and aortic insufficiency.

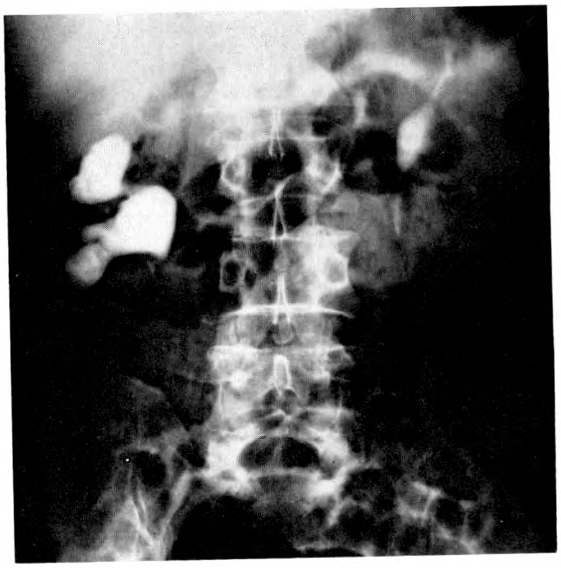

FIG. 5. Congenital ureteropelvic obstruction on the right demonstrated on a postangiographic pyelogram of a patient with pulmonary disease.

ogy demonstrated in this series was 1.4 per cent at the Yale-New Haven Medical Center and 10.0 per cent at the West Haven Veterans Administration Hospital. It is of interest that in the latter group of patients, who had examinations only for acquired pulmonary and cardiovascular diseases, the congenital lesions uncovered by the postangiographic pyelogram were twice as common as those of acquired urinary tract pathology.

Prior to the routine use of postangiographic pyelography, instances were found where excretory urography became necessary several years after angiocardiography and subsequent surgery for a cardiac defect. These urinary abnormalities could have been known earlier and the problems anticipated before the onset of urinary symptoms had a postangiographic pyelogram been made. In certain patients, the findings in the postangiographic pyelogram have led to further investigations of the urinary tract.

A search for abnormalities need not be the main purpose of the postangiographic pyelogram. Since the delayed abdominal roentgenogram is a rough index of renal function and anatomy, it complements other studies in the complete evaluation of the patient, especially in those who may undergo surgery. Furthermore, the post-

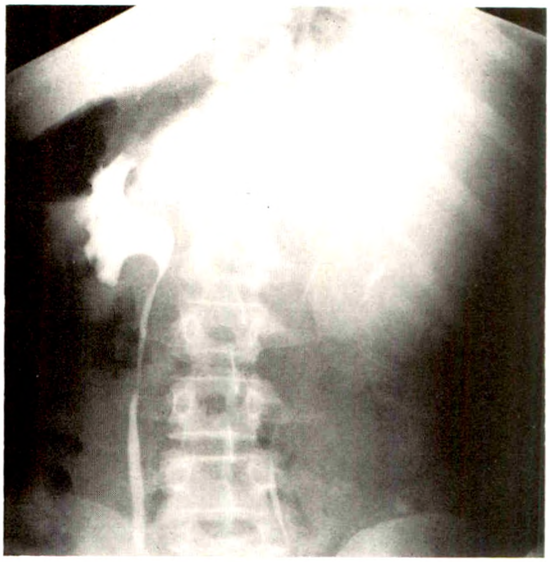

Fig. 7. Postangiographic pyelogram showing apparent enlargement and medial displacement of the left kidney by splenomegaly in a patient who had transhepatic venography for postnecrotic cirrhosis.

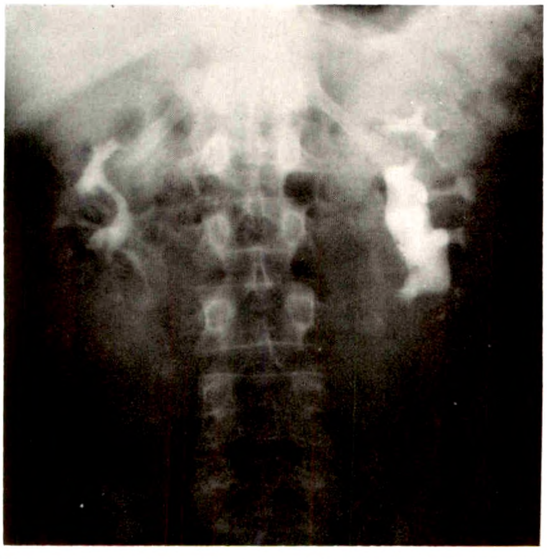

Fig. 6. Partial malrotation of the left kidney seen in a patient after pulmonary arteriography for a chest lesion.

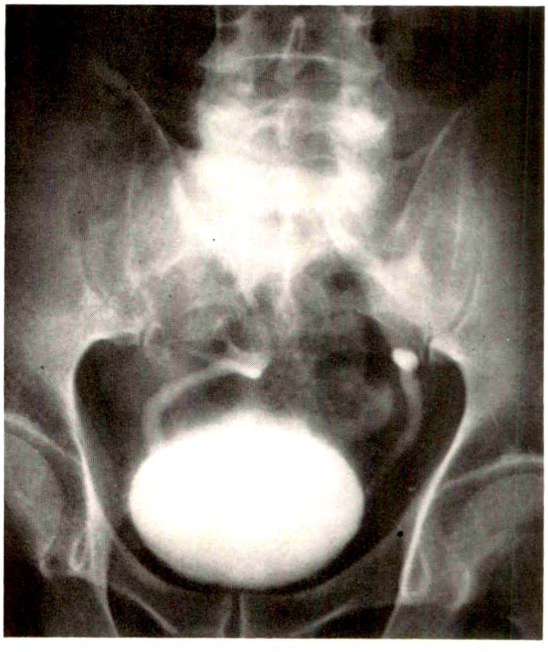

Fig. 8. Bilateral pelvic kidneys detected in an elderly patient who had femoral arteriography for intermittent claudication of the lower extremities.

TABLE I

INCIDENCE OF URINARY TRACT DISEASES DETECTED BY THE POSTANGIOGRAPHIC PYELOGRAM

Angiographic examination for	Yale-New Haven Medical Center			West Haven Veterans Administration Hospital		
	No. of Examinations	Kidney Lesions		No. of Examinations	Kidney Lesions	
		Congenital	Acquired		Congenital	Acquired
Congenital heart disease	493	12				
Acquired heart and pulmonary diseases	367		3	44	4	1
Others, excluding examinations of the abdominal aorta and branches	373	2		46	2	2
Total	1233	14	3	90	6	3
Incidence		1.4%			10.0%	

angiographic pyelogram may be utilized for comparison to a study which may be required in the future.

A poor pyelogram is ordinarily expected following the enteric introduction of radiopaque contrast material. However, the demonstration of a fairly good excretory urogram in such instances may be a clue to the probable presence of disruption in the continuity of the alimentary tract, accounting, therefore, for the absorption of a sufficient amount of iodinated material.[1]

If excretory urography and angiography are contemplated in the same patient, pyelograms obtained after the angiographic procedure prove more economical in money, time and preparation. Also better anatomic detail may be secured in this study than in the regular intravenous pyelogram, due to the larger dose of radiopaque contrast medium used.[2]

SUMMARY

The value of the postangiographic pyelogram is emphasized. Urinary abnormalities detected by this means are shown in accompanying roentgenograms and are tabularly compiled.

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TABLE II

URINARY TRACT PATHOLOGY DEMONSTRATED BY THE POSTANGIOGRAPHIC PYELOGRAM

Congenital Anomalies	Yale-New Haven Medical Center	West Haven Veterans Administration Hospital
Agenesis of one kidney	3	
Hypoplastic right kidney	1	
Horseshoe kidneys	3	
Malrotation		1
Retrocaval ureter	2	
Vesical diverticula	1	
Pelvic kidneys	1	
Double or bifid ureters	2	3
Ureteropelvic obstruction	1	2
Total	14	6
Acquired Diseases		
Renal carcinoma	1 (proved)	1 (unproved)
Deviated ureter by lymphosarcoma		1
Enlarged and displaced kidney by hepatosplenomegaly from liver cirrhosis	1	1
Renal artery stenosis (contracted kidney)	1	
Total	3	3

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FIBROMUSCULAR HYPERPLASIA OF THE ILIAC ARTERY

A CASE REPORT

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FIBROMUSCULAR hyperplasia of the renal arteries as a cause of hypertension has been well documented in the literature. We have had the opportunity to observe a patient with fibromuscular hyperplasia of both renal arteries as well as of the right external iliac vessel. The purpose of the authors is to report this case and to discuss the possible developmental mechanisms of this disease.

Leadbetter and Burkland[2] first described the entity in a 5 year old Negro male in 1938. Since then, DeCamp and Marshall, Poutasse and Dustan, Wylie and Wellington, and other authors[3,4,6,7] have confirmed its presence.

The preponderance of cases occurring in young females who have been pregnant has been noted. Until recently, fibromuscular hyperplasia was thought to occur only in the main and accessory renal arteries. The patients studied usually presented with a milder degree of hypertension than those with atherosclerosis of the main renal arteries. The total renal function studies tend to be normal, whereas they are abnormal in patients with atherosclerosis. An abdominal bruit is heard in both types of renovascular stenosis with marked regularity. In general, the stenotic lesion is found to be due to hypertrophy of the musculature and, to a lesser degree, the fibrous connective tissue elements of the media of the vessel (Fig. 1).

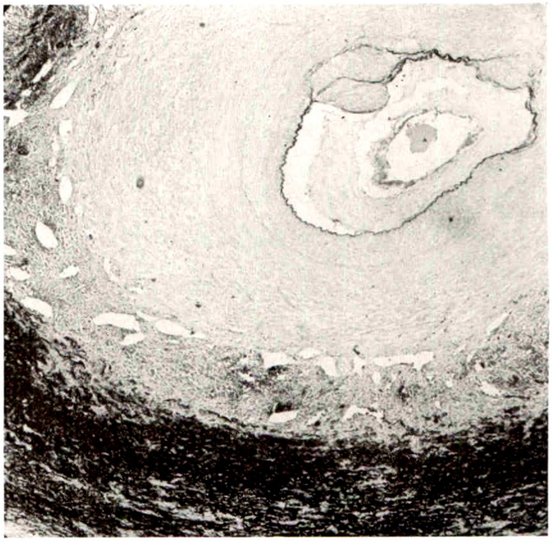

Fig. 1. Photomicrograph of cross section of a vessel showing marked hypertrophy of the muscular layer.

REPORT OF A CASE

A para III gravida III 43 year old white female was first admitted to Georgetown University Hospital for evaluation of hypertension. Seven years prior to admission, the patient had considerable edema during her third pregnancy and was placed on a low salt regimen. Hypertension was not documented at this time. Following this pregnancy, the patient had recurrent bouts of middle ear infections, but was relatively well until 6 months later when she experienced an episode of excruciating chest pain, lasting 45 minutes. She was hospitalized at another hospital for 3 weeks, and was told she had had a heart attack. She was advised to rest for 3 months, but was not placed on any medication. Since then, she has had no limitation of activities, which include swimming and dancing.

Two years prior to admission, the patient was found to be hypertensive on a physical examination before cystoscopy. She was treated for a urethral stricture, and has had no recurrence. She denied having headaches, but had complaints of dyspnea on exertion (one flight of stairs), chest pain, chills, fever, dysuria, and hematuria or colored urine. The patient had not been on antihypertensive medication or digitalis. There was no family history of hypertension. An intravenous pyelogram, at another hospital, made 2 weeks prior to admission, was reported as abnormal.

Physical examination revealed an alert, well-nourished white female in no distress. The blood pressure in the right arm was 150/100 sitting, 135/90 standing; in the left arm 150/100 sitting; and a 180 systolic pressure was noted in the right leg. Examination of the head and neck was negative. The lungs were clear to ausculation and percussion. Examination of the heart revealed the point of maximal impulse 2 cm. to the left of the mid-clavicular line. There was a regular sinus rhythm. No thrills, murmurs or rubs were heard. A systolic bruit was heard in the abdomen, 3 cm. to the left of the umbilicus. The liver, kidneys and spleen were not palpable. Examination of the extremities revealed a right femoral bruit; however, both femoral and radial pulses were equal bilaterally. There was a one plus pedal edema bilaterally.

Laboratory examination revealed the total renal function studies to be essentially normal. A translumbar aortogram, however, demonstrated the characteristic appearance of fibromuscular hyperplasia in both renal arteries, as well as in the right external iliac artery (Fig. 2 and 3).

The patient was operated upon and a plastic repair of the left renal artery was performed. She tolerated the procedure well. The postoperative blood pressure was consistently in the normotensive range. A similar surgical procedure may be performed at a later date on the right renal artery, if warranted.

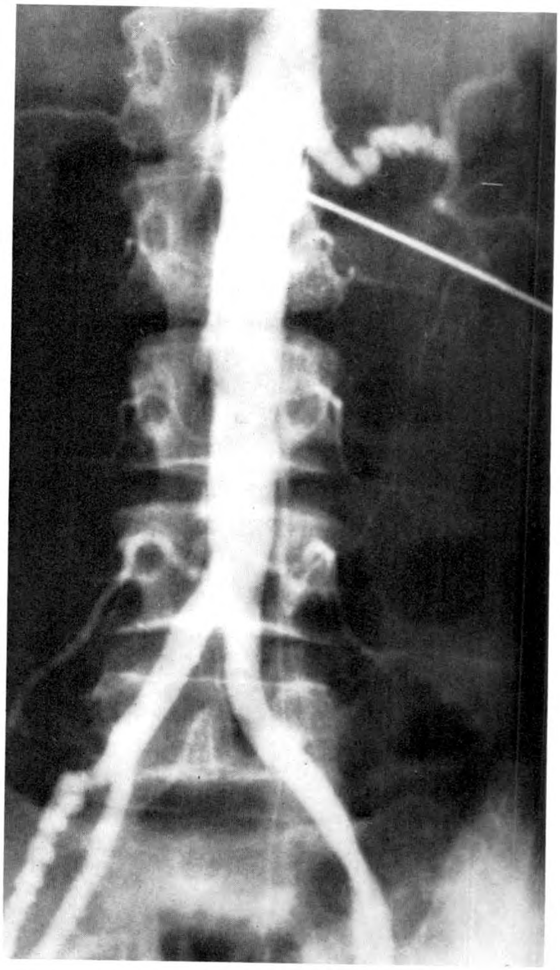

Fig. 3. Translumbar aortogram revealing typical beaded appearance of fibromuscular hyperplasia in the right external iliac artery as well as in the left renal artery.

COMMENTS

This case presented the rather typical history, physical, laboratory and roentgenographic findings of hypertensive patients with fibromuscular hyperplasia of the renal arteries. The unusual occurrence of this disease process in the right external iliac artery, though not proved pathologically, is evidenced by the femoral bruit, characteristic roentgenographic findings and the presence of the disease elsewhere in the renal arteries. The surgical management of this patient has resulted in a normotensive individual, but residual disease remains. Since progression of the disease is known to occur, future surgery of the right renal artery and a plastic repair of the external iliac artery may be necessary.

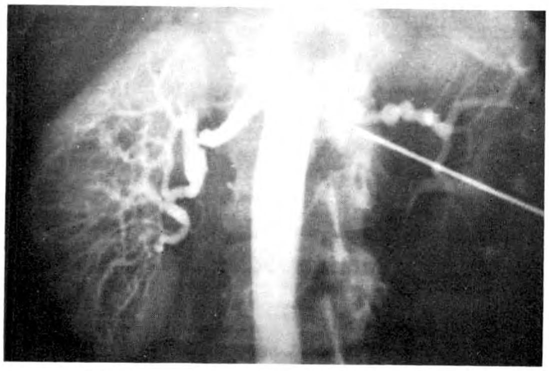

Fig. 2. Translumbar aortogram showing fibromuscular hyperplasia involving both renal arteries but most prominently on the left side.

DISCUSSION

Various theories concerning the etiology of fibromuscular hyperplasia have been advanced. A congenital deficiency of the elastica in the media of the vessels has been suggested. No evidence of support for an endocrine, inflammatory, or collagen basis has been found. Palubinskas and Wylie[4] in 1961 were of the opinion that chronic stretching of the renal arteries in patients with very mobile kidneys induced hyperplasia. This would account for the fact that more females than males are affected as pregnancy would produce additional stretching and tension of the renal arteries. Since the extrarenal occurrence of the disease has been reported, they now feel that fibromuscular hyperplasia perhaps represents a generalized arterial dysplasia rather than a process limited to the renal arteries.

The occurrence of fibromuscular hyperplasia primarily in the renal arteries and, to a lesser degree, in the various immediate branches of the aorta, but not in the smaller, more distal arterioles, may possibly be explained on the basis of mechanical alteration to flow at or near the point of junction of these vessels with the aorta.

The large "elastic" conducting arteries such as the aorta and its main subdivisions differ histologically from the muscular distributing arteries in having considerably more connective tissue (collagen and elastica) in their walls. Yet as the excellent review of Benninghoff in 1930 indicates, there is no sharp line of demarcation.[1]

The elastica provides the reversible extensibility characteristic of normal blood vessels, offering long range movement, rebound, and shock absorption, thereby dampening or decreasing the magnitude of vibrations. Through its distensibility, the elastica offers a resilient reservoir which stores much of the potential energy of the heartbeat in the walls of the aorta and large arteries. During ventricular diastole, the stretched elastic elements of the large arteries shorten as the blood escapes through the arterioles. The strong intermittent cardiac pulsations are thereby converted by the elastica into a modulated pressure pulse providing a relatively continuous and smooth delivery of blood to the tissues.

Like the other connective tissues which arise from the embryonic mesenchyma, the vascular system adapts in specific ways to the mechanical forces which act upon it (Table I) (Redbard, 1956; Brenner, 1932).[1]

For example, stretching of fibroblasts in tissue culture results in an increase rate of multiplication, with the cells becoming oriented in lines parallel to the direction of strain (P. Weiss, 1939; Fell, 1951).[1] As a consequence, the collagen which is formed is aligned with the tensile forces, and the cells are relieved of the stretching force. This constitutes a feed back mechanism whereby strain on the fibroblast leads to the production of a material which takes up the strain and removes the force from the cell. Similar cybernetic mechanisms appear to be operative in response to other forces.

Thus, fibroblasts under tensile stress secrete collagen, the amount of which in a vessel varies with the peak mechanical tension on the wall. Enhanced amounts of collagen fibers are evident at sites of increased stress, as at branchings of vessels and the roots of the valves. While collagen limits the degree of distention of a vessel, it

Table I

EFFECT OF MECHANICAL FORCES IN STRUCTURE OF VASCULAR SYSTEM

Force	Response
Pressure	Filtration, tension compression
Transmural pressure	Wall strength
Tension	Reticulum collagen, muscular hypertrophy
Rate of change of tension	Hyaline elastica
Compression	Osteoid, bone
Rate of change of compression	Cartilage
Increased flow	Enlargement of the lumen
Decreased flow	Subendothelial proliferation

does little to modify or dampen the pulsatile forces of the arterial system.

Muscles occur only in the media, being absent from the intima and adventitia. In a blood vessel, contraction of the muscle reduces the lumen, thereby increasing the blood pressure which re-elongates the muscle.

The smooth muscle also contributes to the elastic properties of the vessel wall. As with the collagenous elements, the amount of smooth muscle in the vessel wall depends upon the amount of force acting against it.

Most of the stress on the vessel wall is sustained by the media as the intima and adventitia have little strength.

PHYSICS OF BLOOD FLOW

The dynamics of the cardiovascular system are complex and one is referred to the excellent work by Rouse, Prandell and others for more detailed study.[1] Fundamentally, the stress on the vessel wall is dependent in large part upon the size of the orifice, velocity of flow of the blood through the vessel, amount of turbulence and the vascular resistance in the peripheral bed being supplied. A larger orifice results in a more rapid arterial flow, and thus little force driving the blood is applied to the vessel walls. This is true unless substantial resistance is encountered in the peripheral vascular bed.

With obstruction of the flow, the kinetic energy in the forward movement of the stream is converted, in large part or all, to distending pressure. Thus, both experimental and clinical evidence shows that stenotic or coarcted lesions result in an intimal proliferation to some degree. An even greater degree of proliferation occurs in the fibrous and muscular elements of the wall. This, in fact, further compromises the arterial lumen, resulting in more stenosis and thus a vicious cycle is commenced. Beyond the stenotic lesion, jet streams and turbulence further influence the character of the vessel wall. Hypertrophy cannot keep pace with the direct force of the jet. The wall becomes stretched and aneurysmal dilatation ensues. The stress is great at the junction of the normal wall with the dilated segment. As a result, the normal vessel tends to be incorporated in the aneurysm. When the ends of an ectatic vessel are at fixed distances from each other, lengthening becomes apparent as an increasing tortuosity of the vessel. In this way, the pathologic and the roentgenographic findings of beaded, or multiple saccular aneurysmal, and tortuous renal arteries may be explained.

Another factor to be considered is the general lack of peripheral arterial bed resistance peculiar to the kidney and, perhaps, to a lesser extent in the internal carotid artery. We have reviewed roentgenograms of a case of fibromuscular hyperplasia of the internal carotid artery. This condition, under normal circumstances, accounts for a greater velocity of blood flow through the vessel, and thus there is less lateral wall pressure. Therefore, when constriction takes place in this type of vessel, the response in the fibromuscular wall might well be expected to be greater than elsewhere.

Still another factor to be considered is that of the aging process. With advancing age, there is a loss of the elastic elements of the media and increase in collagenous elements. This results in less distensibility of the wall. Hence, we see the elevated systolic pressures and wider pulse pressure in elderly individuals. This loss of the elastic elements and replacement by collagenous tissue may account for the rarity of the fibromuscular lesion in elderly patients. The constricting lesion in the elderly patient evokes an arteriosclerotic response, especially in the pressure of excessive circulating lipids. Thus, intimal and medial degeneration with collagen formation in the media dominates the pathologic picture.

Accordingly, fibromuscular hyperplasia would be most likely to appear in:

1. The immediate branching high flow arteries of the aorta where, at least, some elastic elements, as well as muscular

elements, are present in the media.

2. A relatively mobile, small lumen vessel which may kink under some circumstances and interrupt the normal flow phenomenon. This could conceivably initiate a fibromuscular medial response and thus may account for a high susceptibility in females, especially those having the additional compression effects of pregnancy.

3. A pre-arteriosclerotic age group wherein the media has not lost its elastic element.

4. Vessels which have a normal lack of peripheral vascular bed resistance. In these instances partial obstruction of the lumen producing fibromuscular hyperplasia would be possible.

In the order of frequency, occurrence of the disease in the various branches of the aorta would be as follows depending upon the presence or absence of the above factors:

1. Renal arteries in females. These vessels seem to best satisfy all the above conditions. Certainly, the mobility of the kidney and the added compression and torsion effects of pregnancy are apparent. The vessel has a high flow rate in spite of its small orifice due to lack of peripheral bed resistance.

2. Superior and inferior mesenteric arteries and the celiac axis. There is certainly a fair degree of mobility in the superior and inferior mesenteric arteries, and, to a lesser degree, in the celiac artery. However, though the vascular bed resistance is higher in the superior and inferior mesenteric arteries, it is somewhat less in the celiac artery and these two factors may counteract each other and the frequency of occurrence may be approximately the same in these 3 arteries.

3. External iliac vessel. This vessel branches at an acute angle from the common iliac artery, as opposed to the hypogastric artery. With the additional compression effects of pregnancy, one can easily see how the process can be initiated here in spite of a relatively large lumen.

4. Hepatic and splenic arteries. The hepatic and splenic arteries, though somewhat less mobile than the renal and superior mesenteric arteries, have sufficient length as well as relatively small lumina to become partially obstructed, thus initiating the disease process. The peripheral resistance of both, however, is somewhat higher than that of the renal and carotid arteries.

5. Internal carotid artery. This vessel has a large lumen and probably less mobility than some of the others. The high velocity of flow in this vessel, both because of lumen size and lack of peripheral bed resistance, combined with a small amount of distortion of the vessel would cause severe pressure directly on the vessel wall at the disturbance site, thus initiating the process.

6. The lumbar vessels. Because of their relatively short, fixed position, and relatively high bed resistance and low flow characteristics, these vessels are less likely to be affected by fibromuscular hyperplasia.

7. Inferior phrenic arteries. Though these vessels have a certain amount of normal mobility, the high bed resistance and low flow characteristics would make these vessels less likely to develop the disease process.

8. Suprarenal, internal spermatic, and ovarian arteries. Because of low flow characteristics, fibromuscular hyperplasia would be less likely to develop in these arteries.

9. Coronary arteries. These vessels, though undergoing a great deal of constant stretching, shortening, and torsion, are very unlikely to develop fibromuscular hyperplasia. Because of their anatomic relationship to the surrounding myocardium, they are, in a sense, in a fixed position, and therefore not apt to develop a long-lasting constricting or torsion type lesion.

SUMMARY

A patient with typical symptomatology, laboratory and roentgenographic findings

of fibromuscular hyperplasia of both renal arteries is reported. The additional finding of the disease in the iliac vessel is noteworthy. Fifteen to twenty-eight per cent of patients with hypertension due to renal artery stenosis are found to have fibromuscular hyperplasia. It is emphasized that this disease may present itself in extrarenal vessels. With improved diagnostic and surgical techniques, treatment of the disease is possible wherever it manifests itself. The developmental mechanisms of the disease and the probability of occurrence in various vessels are discussed.

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FINDINGS ON EXCRETORY UROGRAPHY CLOSELY FOLLOWING EXTRAVASATION OF CONTRAST MATERIAL FROM THE PELVIC URETER

By D. R. McFARLANE, M.D.
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ALL radiologists are familiar with the relatively common occurrence of extravasation of contrast medium in the region of the vesicoureteral junction during attempted ureteral catheterization and retrograde pyelography. In most instances, the ureteral perforation occurs at the site of ureteral disease such as an impacted stone, infection or stenosis.[1,6] The frequency of ureteral perforation increases when specialized catheters such as stone extractors, bulb catheters, metal tip catheters, etc., are used. It is likely that extravasation very frequently occurs in the absence of complete penetration of the ureteral wall by the catheter tip. A small defect in the ureteral mucosa may develop secondary to an abrasion from the catheter tip, ureteral distention, or other unknown factors and allow the contrast material to extravasate submucosally. Four types of extravasation frequently seen near the vesicoureteral junction have recently been described and illustrated by Friedenberg and Ney.[2] These are: (1) submucosal; (2) intramural; (3) subserosal; and (4) retroperitoneal extravasations.

Following ureteral perforation or laceration of the ureteral mucosa and extravasation of contrast material in this area, the vast majority of ureters heals spontaneously without specific therapy. Although one would expect at least a temporary abnormality to be produced in the adjacent ureter and bladder by such an extravasation, no reference could be found in the English literature to the changes produced in the excretory urogram or cystogram by this complication. This is perhaps related to the infrequency with which these examinations are performed immediately following traumatic ureteral catheterization and extravasation. Since the changes may simulate other conditions such as ureteral obstruction and bladder neoplasm, and since the history of recent perforation may not always be available when interpreting the excretory urogram, radiologists should be aware of the appearance that may result and keep this possibility in mind.

REPORT OF CASES

Case 1. This 62 year old white male was admitted to St. Lawrence Hospital on November 8, 1961 because of pain in his back and right flank and a "polyp in the colon." Physical examination disclosed only slight right flank tenderness and benign prostatic hypertrophy. There were occasional red blood cells and 5 to 7 white blood cells per high power field in the urine. A blood count was normal. A barium enema study disclosed a 2.5 cm. polyp in the ascending colon which was unchanged since an examination 3 months earlier.

On November 9, 1961, cystoscopy was performed under general anesthesia. A urethral stricture was present. No bladder abnormality was described but the enlarged prostate was causing partial urethral obstruction. The right ureter was catheterized easily, but all efforts to catheterize the left ureter were unsuccessful and contrast material injected into the left ureteral orifice flowed back down around the catheter. A roentgenogram obtained at this time (Fig. 1) demonstrated extravasation of contrast material arising from the intramural portion of the left pelvic ureter. The examination was terminated and excretory urography was requested and performed about 4 hours later. The extravasated contrast material had completely absorbed when the preliminary roentgenogram was obtained. The upper urinary tracts were grossly normal and there was no ureteral obstruction. On the 10 minute study (Fig. 2), a filling defect in the left wall of the bladder was obvious and remained constant on roentgenograms made at 12, 15 and 60 minute intervals. The patient then voided but a postvoiding cystogram (Fig. 3) demonstrated considerable bladder residual as well as the filling defect.

No urinary tract problems developed following this procedure and the patient was discharged on November 25, 1961 at which time he had no specific urinary symptoms.

CASE II. A 56 year old white male was admitted to St. Lawrence Hospital on December 28, 1961 because of gross hematuria. He had experienced occasional nocturia and dysuria for several months. Physical examination was negative except for moderate prostatic enlargement without evidence of malignancy. Urinalysis and a complete blood count were normal. Cystoscopy was performed under general anesthesia on December 29, 1961. The cystoscopist described enlargement of the median bar and median lobe of the prostate, and the mucosa over the enlarged portions bled easily. There was no evidence of bladder tumor. Despite several attempts, a catheter could not be passed up the left ureter. Contrast material was then injected into the left ureteral orifice through a small bulb pine cone catheter and a roentgenogram was obtained (Fig. 4). The extravasation of contrast medium from the intramural portion of the left ureter was noted and the procedure was terminated.

Excretory urography was done later the same day. The extravasated contrast material was no longer visible; however, there was partial obstruction of the intramural portion of the left ureter and a filling defect in the left bladder wall (Fig. 5). In 1 hour, extravasation of contrast material was again noted outside the lumen of the left pelvic ureter (Fig. 6 and 7).

The subsequent course was uneventful and

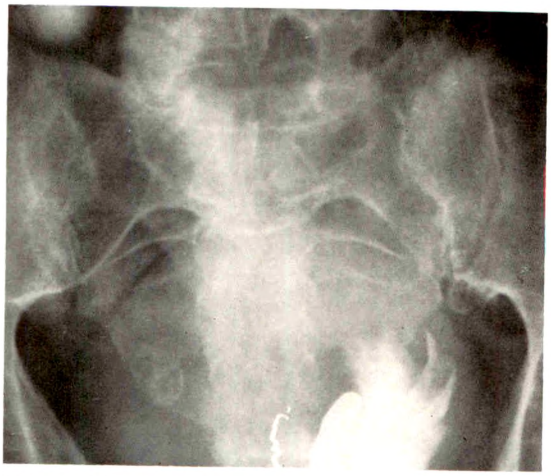

FIG. 1. Case I. Extravasation of contrast medium around left pelvic ureter following unsuccessful ureteral catheterization.

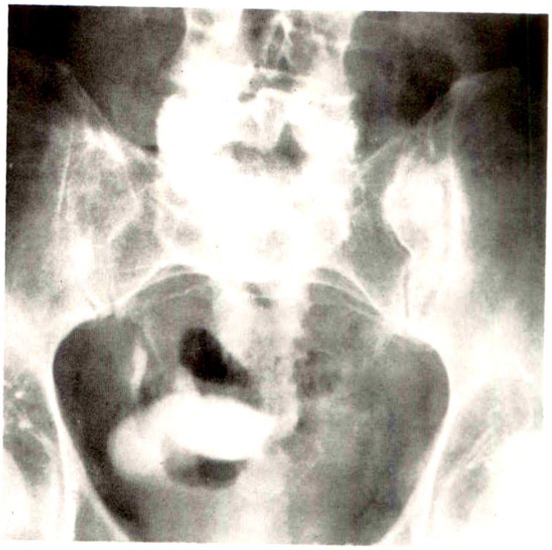

FIG. 2. Case I. Ten minutes after injection of 50 per cent hypaque, a filling defect is seen in the left bladder wall and the bladder appears elevated. There is no ureteral obstruction or extravasation.

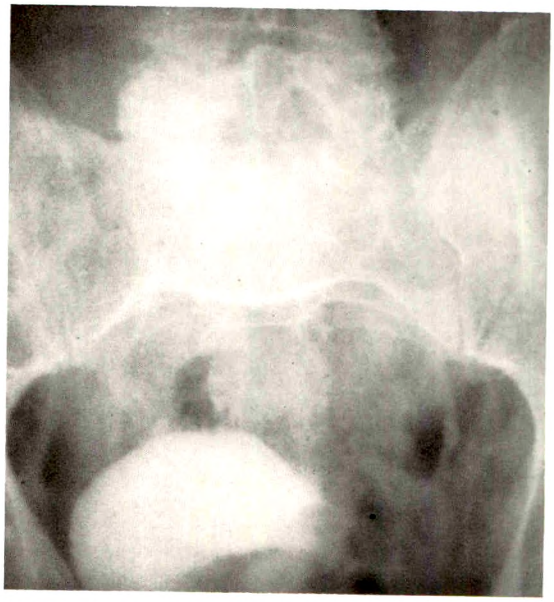

FIG. 3. Case I. After attempted voiding, an obvious filling defect remains in the bladder inferiorly on the left. The patient was able to void only a small amount.

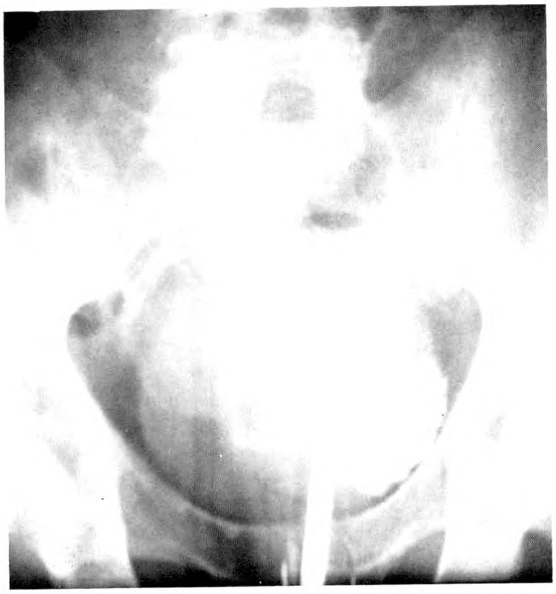

Fig. 4. Case II. Extravasation of contrast medium following unsuccessful left ureteral catheterization and retrograde pyelography.

the patient was discharged on December 30, 1961 at which time he was reportedly "voiding without difficulty."

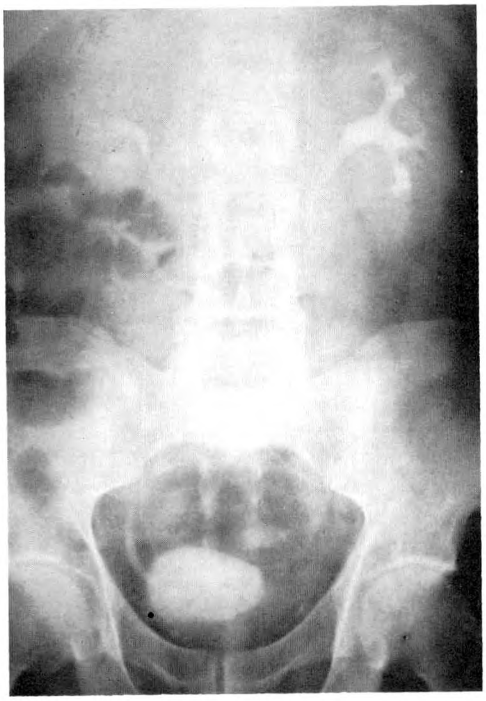

Fig. 5. Case II. Ten minute study from an excretory urogram. Filling defect seen in left urinary bladder and slight dilatation of left upper collecting system. No extravasated contrast medium is visible.

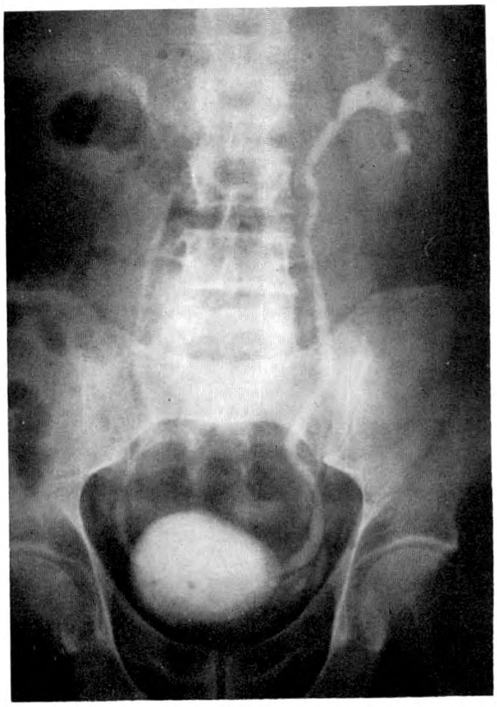

Fig. 6. Case II. One hour urogram shows obstruction of the distal left ureter and contrast medium extravasation. Bladder filling defect again seen.

DISCUSSION

Most urologists now consider instrumental ureteral perforation and extravasation a relatively benign complication, but prior to the availability of antibiotics, this was regarded as a potentially dangerous situa-

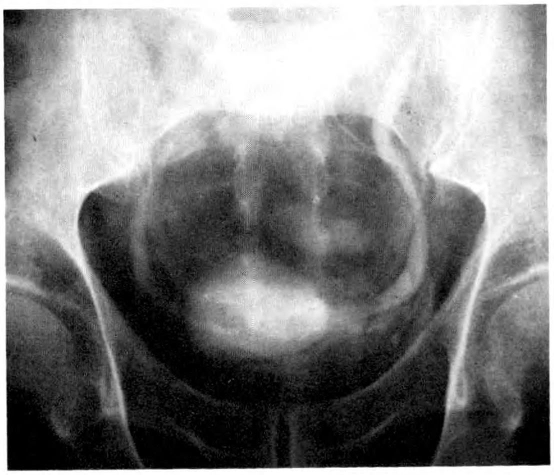

Fig. 7. Case II. Postvoiding roentgenogram showing ureteral obstruction, extravasation of contrast medium, and deformity of the urinary bladder.

tion. The described cases indicate that a significant localized reaction is produced at the site of extravasation and may lead to a mass in the region of the ureterovesical junction, probably resulting from edema, hemorrhage, and/or spasm. The duration of these changes is unknown but they are undoubtedly temporary in view of the frequency of periureteral contrast extravasation and the infrequency of serious complications.

Unless specialized catheters have been used, a complete perforation of the ureteral wall by the catheter will nearly always indicate an abnormal ureter at that point. Many urologists believe, however, that a mucosal tear in the ureter may occur even when ordinary catheters are used and allow extravasation of contrast medium out of a normal ureter even though the catheter tip has penetrated no more than the mucosal layer or perhaps merely scratched the mucosa. In an experimental study, Wesson[6] was unable to perforate the normal ureter in fresh necropsy specimens using ordinary catheters. Perforation may follow repeated attempts at ureteral catheterization when there is insufficient time between instrumentations for the ureter to recover.[5] A stone impacted in the distal ureter may predispose the ureter to spontaneous or instrumental perforation. An unusually large stone in the terminal ureter may produce a filling defect in the urinary bladder by direct extrinsic pressure on the bladder wall.

Excretory urography is the most readily available method in diagnosing ureteral injuries and also provides a guide to therapy.[4] More frequent use of excretory urography following surgical procedures on the lower urinary tract would probably show the frequency of complications to be greater than is clinically suspected. Early demonstration of these injuries would allow appropriate therapy to be instituted promptly.

SUMMARY

1. Laceration of the ureteral mucosa or perforation of the ureter during ureteral catheterization with subsequent extravasation of contrast medium is a relatively frequent complication of retrograde pyelography.
2. No reference to the roentgenographic findings when excretory urography is performed soon after this complication could be found in the English literature.
3. Two case reports are presented which illustrate the findings which may result from this sequence of events.
4. Bladder filling defects simulating carcinoma, ureteral obstruction, and extravasation of the intravenously administered contrast medium about the distal ureter are three findings illustrated by these cases.
5. Complete ureteral perforation by a catheter usually occurs only if the ureter is diseased or damaged or if specialized catheters such as stone extractors and metal tip catheters are used.

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A DEVICE FOR OBLIQUE ROENTGENOGRAPHY WITH URETERAL COMPRESSION DURING INTRAVENOUS UROGRAPHY*

By MARVIN J. FRIEDENBERG, M.D.
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THE quality of intravenous urograms is improved significantly by the application of extrinsic ureteral compression after the injection of contrast material. The usual ureteral compression device attaches to the roentgenographic table, making it impossible to obtain exposures in oblique and other views which require mobility of the patient for positioning. To avoid this inadequacy, Steiner designed a device which girdles the patient, using inflatable pads to compress the ureters.* The purpose of the author is to describe a new ureteral compression device which was designed to permit patient mobility during excretory urography. The compression pressure also is applied by a pneumatic bag, but the device has the added advantage that effective ureteral compression is accomplished by means of cones.

URETERAL COMPRESSION DEVICE

Figure 1, *A*, *B* and *C* shows the ureteral compression device as photographed from 3 aspects. Figure 2 is a mechanical drawing of the component parts, with each part identified by letter. The legend for Figure 2 indicates the materials from which the parts are made. The device consists essentially of two compression cones (C) glued to a platform (A) which moves toward and away from another platform (B) on 4 pins. The pins are glued into holes drilled in platform B. Two straps with buckles (D) or an abdominal binder pass through cut-outs in platform (B) and completely encircle the patient, applying the apparatus to him. After tightening the straps or binder, a bag between the two platforms is inflated, compressing the ureters by forcing the cones into the abdomen. All of the component parts of the apparatus are completely radiolucent with the technical factors used for abdominal roentgenography.†

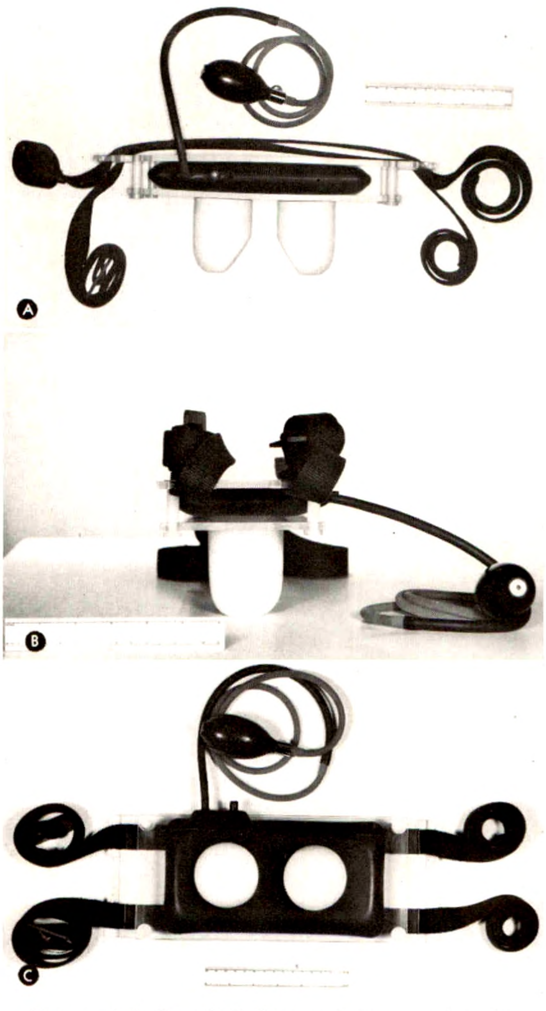

Fig. 1. (*A*, *B* and *C*) Ureteral compression device as photographed from 3 aspects.

Intravenous urography with this com-

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* Elema-Schönander, Stockholm-Solna, Sweden.

† The ureteral compression device is now manufactured by Dick X-Ray Company, 4000 Olive, St. Louis, Missouri.

* From The Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Missouri.

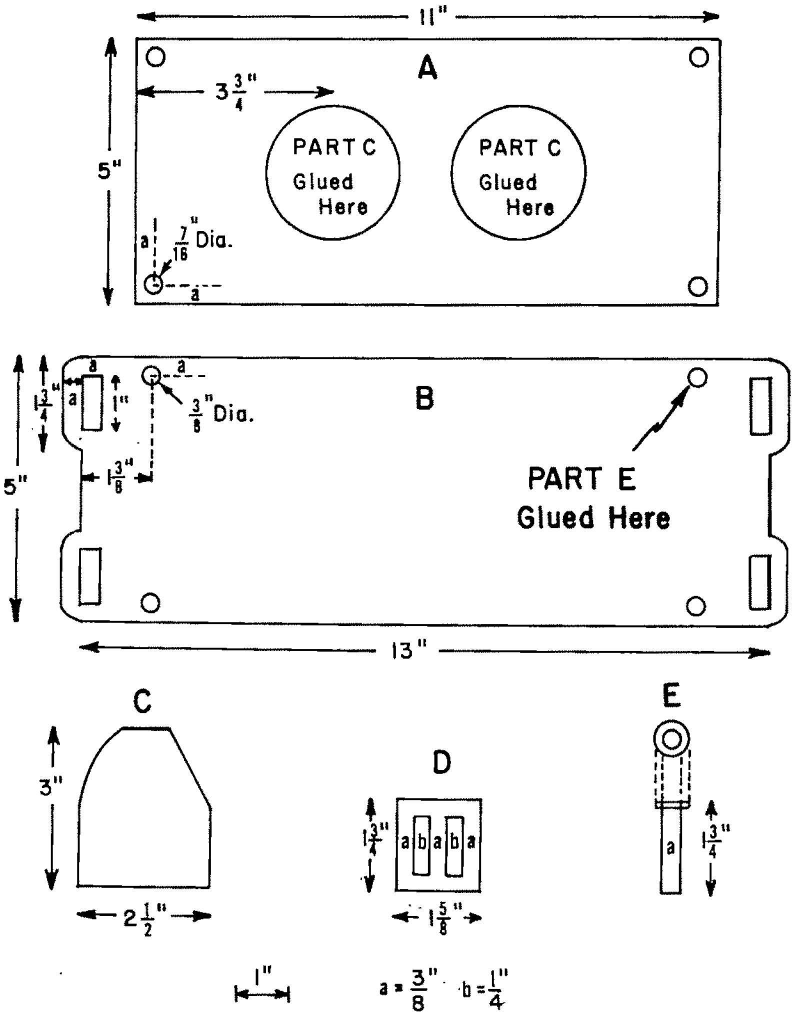

Fig. 2. Mechanical drawing of component parts.

Parts A and B: platforms made from ¼ in. plexiglass, type G unshrunk.
Part C: compression cone made from styrofoam.
Part D: buckle made from ⅛ in. bakelite, cloth laminated preferred.
Part E: pin made from ⅜ in. nylon rod with cap made from ⅛ in. plexiglass.
Straps: 5 ft.×1 in. cotton luggage strapping or Velcro Hook #65 Universal Binder.*
Tycos** latex bag for aneroid sphygmomanometer. Cut off short tube and plug wih nylon plug.
Four foot mayon tubing 3/16 in. internal diameter×1/16 in. wall thickness connects the latex bag to the bulb with a coupling made of nylon.
Parts C and E are glued to parts A and B, respectively, with Rez-n-glue.***

* Westinghouse X-Ray Corporation, 2519 Wilkins, Baltimore 3, Maryland.
** Taylor Instrument Company, 95 Ames Street, Rochester 1, New York.
*** Schwartz Chemical Company, Inc., 50–01 Second Street, Long Island City, New York.

pression device has been performed in over 2,000 patients. The apparatus is well tolerated, and no complications have resulted from its use. The device provides excellent compression of the ureters and urograms of high quality (Fig. 3, *A*, *B* and *C*), particularly when used with high volumes of contrast material.[1] In addition to the preliminary 14 inch×17 inch survey roentgenogram of the abdomen, the follow-

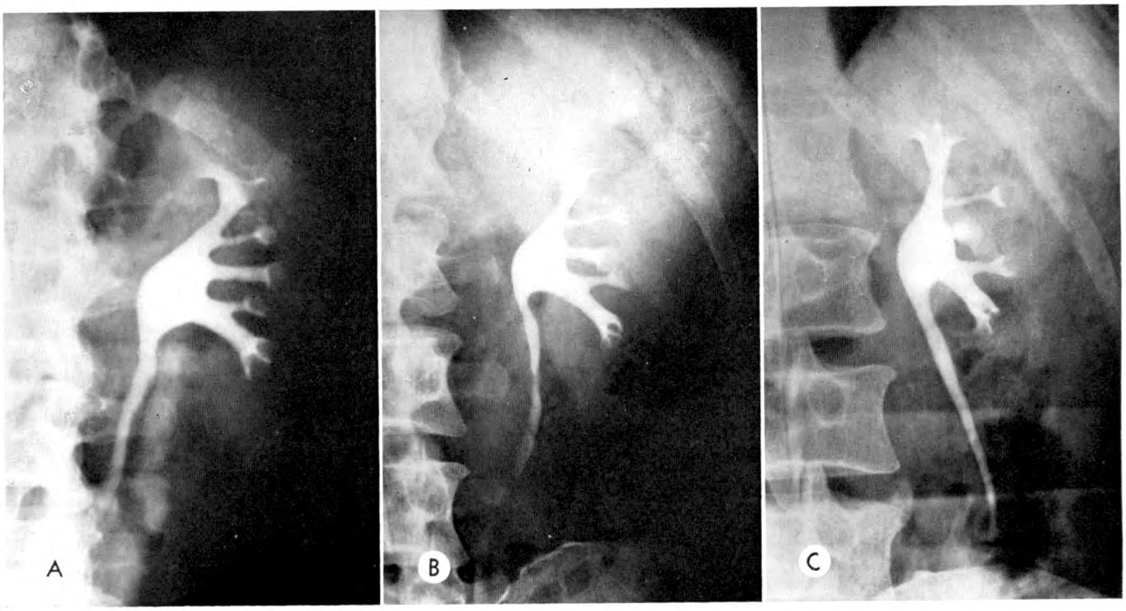

FIG. 3. (*A*) Right posterior oblique, (*B*) anteroposterior, and (*C*) left posterior oblique intravenous urograms of normal left kidney during ureteral compression.

ing roentgenographic program has proved adequate for routine intravenous urography in most patients:

Time	Film Size	Position	Compression
3 min.	14×17 inch	Supine	Off
5 min.	10×12 inch	Supine	On
7 min.	10×12 inch	Right and left oblique	On
10 min.	14×17 inch	Prone	Off
12 min.	14×17 inch	Erect	Off
30 min.	10×12 inch	Supine pre- and post-voiding of bladder	Off

This program is modified or additional views are obtained for the investigation of hypertension, ureteral obstruction, or extrarenal retroperitoneal pathology. The use of high volumes of contrast material and the addition of exposures in oblique projections with ureteral compression have made possible examination of the urinary tract with great confidence in a minimum of time.

CONCLUSION

A new ureteral compression device is described which makes possible complete patient mobility during excretory urography and greatly facilitates examination of the kidneys in a minimum of time.

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The author gratefully acknowledges the assistance of Mr. Harold Smith in the construction of the ureteral compression device described.

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URETERAL COMPRESSION DEVICE FOR EXCRETORY UROGRAPHY

By T. G. DAUGHTRIDGE, M.D.*
PHILADELPHIA, PENNSYLVANIA

THE ureteral compression technique in excretory urography is not new. In spite of numerous publications describing various methods of compressing the ureters, this technique is not widely used and when used, is often not utilized to best advantage. The purpose of the author is to describe a simple and efficient compression device and to again emphasize the necessity of external ureteral compression for a detailed demonstration of the anatomy and pathology of the pelvicalyceal structures.

DESCRIPTION AND APPLICATION OF URETERAL COMPRESSION DEVICE

This device,* a modification of that described by Steinert,[13] is *attached to the patient*, not to the roentgenographic table and has satisfactorily fulfilled our requirements for effective bilateral ureteral compression with a minimum of discomfort. The implement consists of a canvas belt, a plexiglass plate, a block of plastic foam, and two rubber balloons with connecting tubes and an inflation bulb (Fig. 1).

The canvas belt is 5 inches wide and 48 inches long. This is wide enough to minimize pressure over bony protuberances and other pressure sensitive areas and long enough to fit most patients. Additional lengths of belt may be added if necessary. Two nylon strips have been attached to either end of the belt. On one end of the belt, these strips are covered with stiff little hooks and on the other end, the strips consist of soft loops.† These loops and hooks engage one another when pressed together and securely fasten the belt in place until peeled apart. This eliminates the presence of metal buckle shadows and is a simple and effective method of attaching the belt.

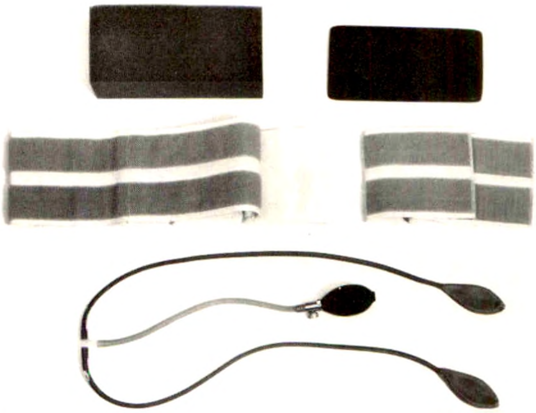

Fig. 1. Components of the compression device (from top left): plastic foam block; plexiglass plate; canvas belt with Velcro strips; additional lengths of belt; balloons, tubing and inflation bulb.

A plexiglass plate, $4\frac{1}{2}$ inches wide and 9 inches long, fits in a pocket near one end of the canvas belt. The length of this plate and the construction of the device is such that pressure is exerted only on the soft tissues between the anterior iliac spines. We have found this one size to be satisfactory in all patients except young children. The plastic foam block is 2 inches thick and slightly wider and longer than the plexiglass plate. The rubber balloons have a 100 cc. capacity and are distended by means of an ordinary manual inflation bulb.

The device is attached to the patient by sliding the belt beneath the hips so the plexiglass plate will overlie the lower anterior abdomen (Fig. 2*A*). The rubber balloons are placed over the lower abdomen on either side of the midline and are covered with the plastic foam block (Fig. 2*B*). The plexiglass is then placed on the foam block

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* Distributed by the Pennsylvania X-Ray Corporation, Glenside, Pa.

† Velcro®, manufactured by the American Velcro Corporation.

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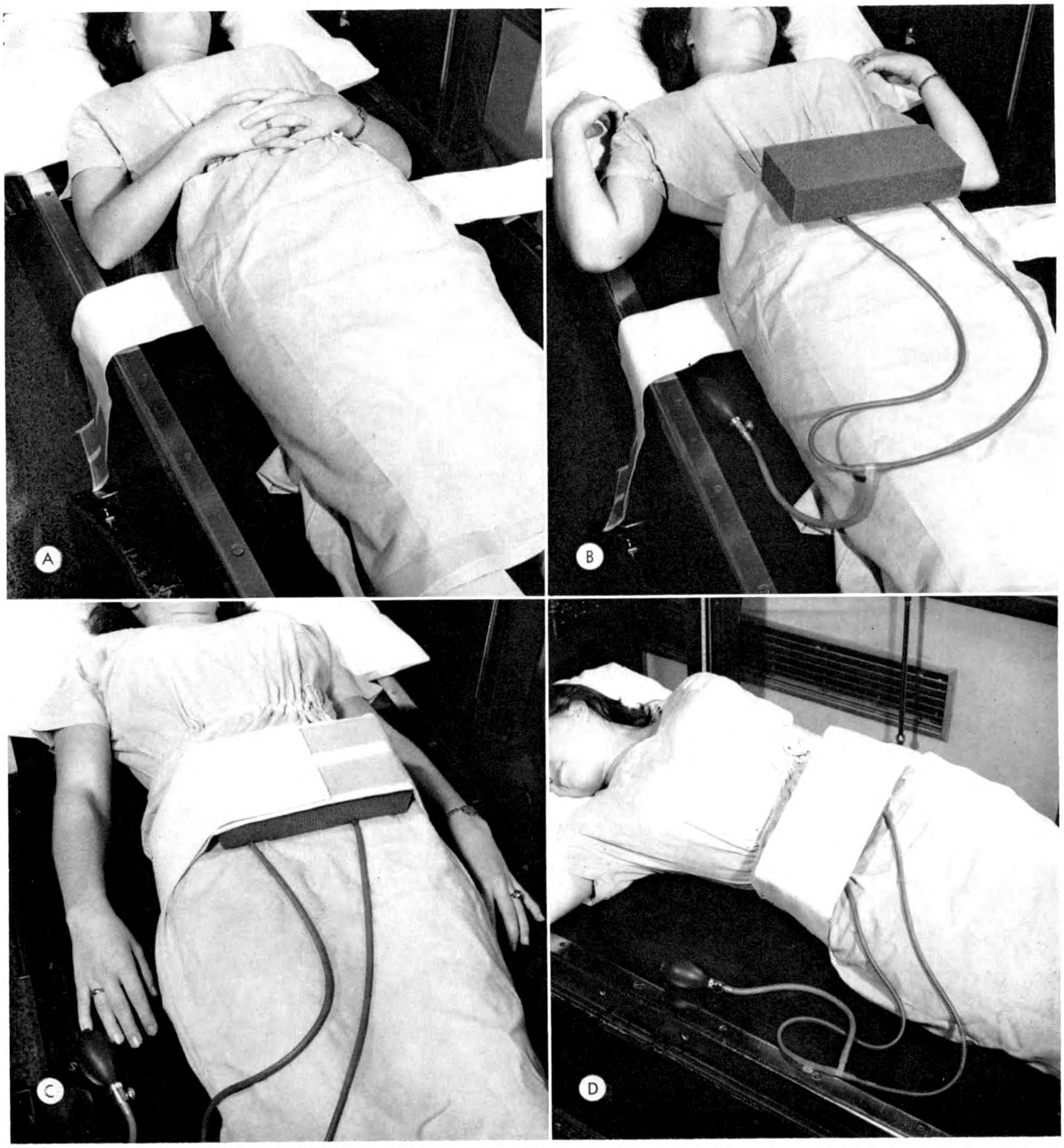

Fig. 2. Application of device. (*A*) The canvas belt is placed beneath the hips so that the plexiglass plate will lie over the lower abdomen. (*B*) The balloons are placed on either side of the midline and the plastic foam block is in place. (*C*) The belt is securely in place, and the patient is positioned for the anteroposterior roentgenogram. (*D*) The patient is positioned for oblique projections with the compression device unchanged.

and with slight pressure, the belt is fastened in position (Fig. 2*C*). The plastic foam serves 2 purposes: (1) to hold the balloons in place and (2) to maintain the tension of the belt, preventing it from slipping about the patient. If the device has been properly placed, inflation of the balloons will result in excellent ureteral compression with minimal discomfort. The patient is free to move about and may be examined in any position necessary (Fig. 2*D*).

No pressure gauge is employed; the patient's tolerance is used as a guide to the amount of compression to use. There have been no instances of hypotension attributable to the belt as mentioned by Olsson,[11] who recommends a predetermined pressure gauge reading.

USE OF THE COMPRESSION BELT FOR EXCRETORY UROGRAPHY

Proper preparation of the patient for excretory urography is still a necessity in spite of the use of compression and the newer contrast agents available. We recommend dehydration of the patient for 12 or more hours and cleansing of the colon by laxatives. We do not use enemas routinely.

Our basic urographic procedure is described below. However, we in no way limit the examination to a specific routine, but vary the procedure to meet the needs of the particular patient.

After the survey examination, roentgenograms of the kidneys are exposed at 3 and/or 5 minutes following the injection of contrast material to demonstrate the presence of function bilaterally. Compression is then applied as previously described and maintained for at least 5 minutes before roentgenograms in frontal and oblique projections of the kidneys are obtained (Fig. 3, *A–D*). Proper application of the compression device is a necessity and this requires a complete understanding of the mechanics and physiology involved by the technologist. As noted by Hamby and Kirsh,[5] the application of pressure to the

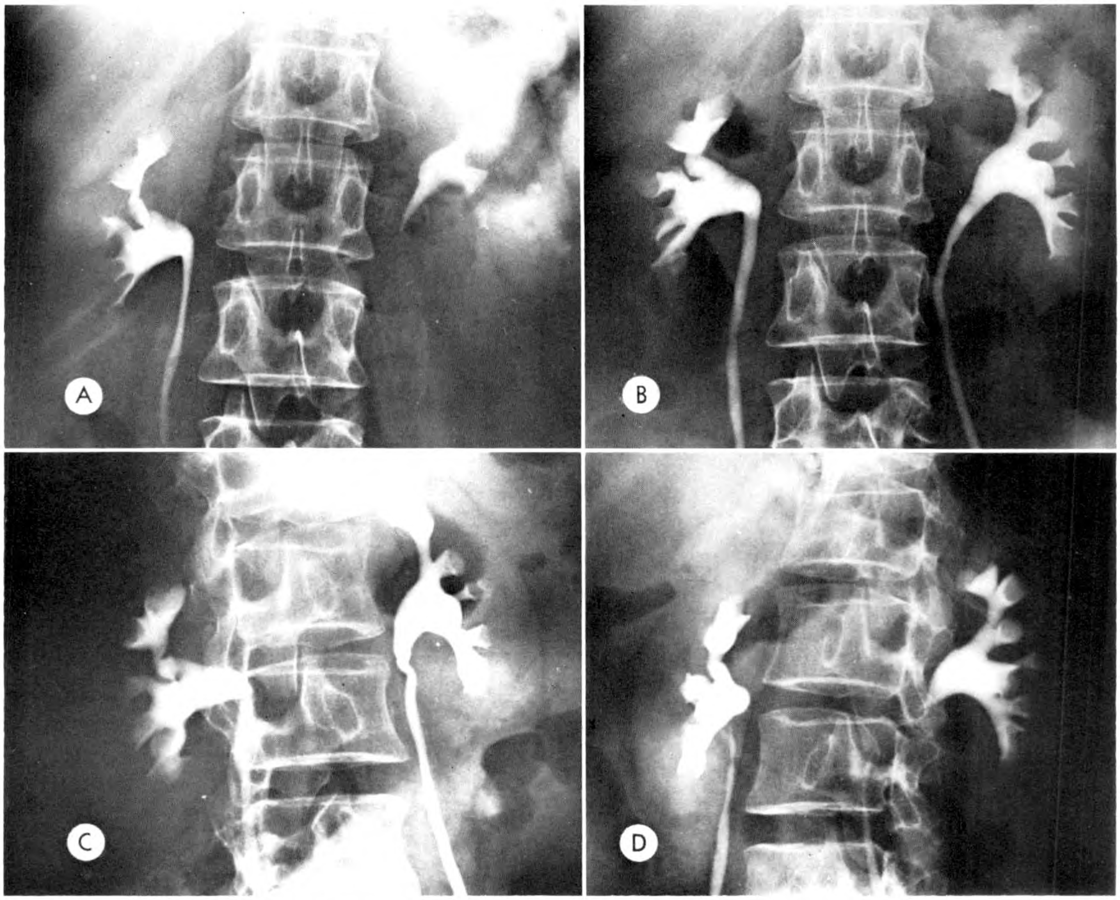

FIG. 3. Normal urograms. (*A*) Without compression, the lower calyceal groups on the left are incompletely filled. (*B*) With compression, all the calyceal groups are well opacified. (*C* and *D*) Oblique roentgenograms with compression showing the value of visualizing the pelves and calyces completely filled in more than one projection.

lower abdomen may decrease femoral pulsations. This is particularly true of our method in older patients with flaccid abdominal musculature. This should be checked for and obliteration of the pulses avoided.

The initial roentgenograms are reviewed by the radiologist, and, if exposures in other projections are necessary, these may be obtained by moving the patient to the desired position with the compression in place. When the kidneys have been satisfactorily demonstrated, the compression is removed. Roentgenograms are made for demonstration of the ureters immediately upon release of the compression, at which time they are usually well opacified. The appropriate bladder roentgenograms are subsequently made.

As stated before, this procedure is varied at any time depending upon the requirements of a particular case. In this respect, another advantage of this device is the ease with which compression may be applied to one side only.

COMPLICATIONS

There have been no complications attributable to the use of this device. Pyelorenal backflow may occur on occasion, but no significant sequela has been noted (Fig. 4, *A*, *B* and *C*).

One patient with a testicular tumor had delayed opacification of the left kidney as observed on the initial roentgenogram (Fig. 5*A*). This suggested the possibility of compression of the major vessels by abnormal lymph nodes at the left renal hilus. In a

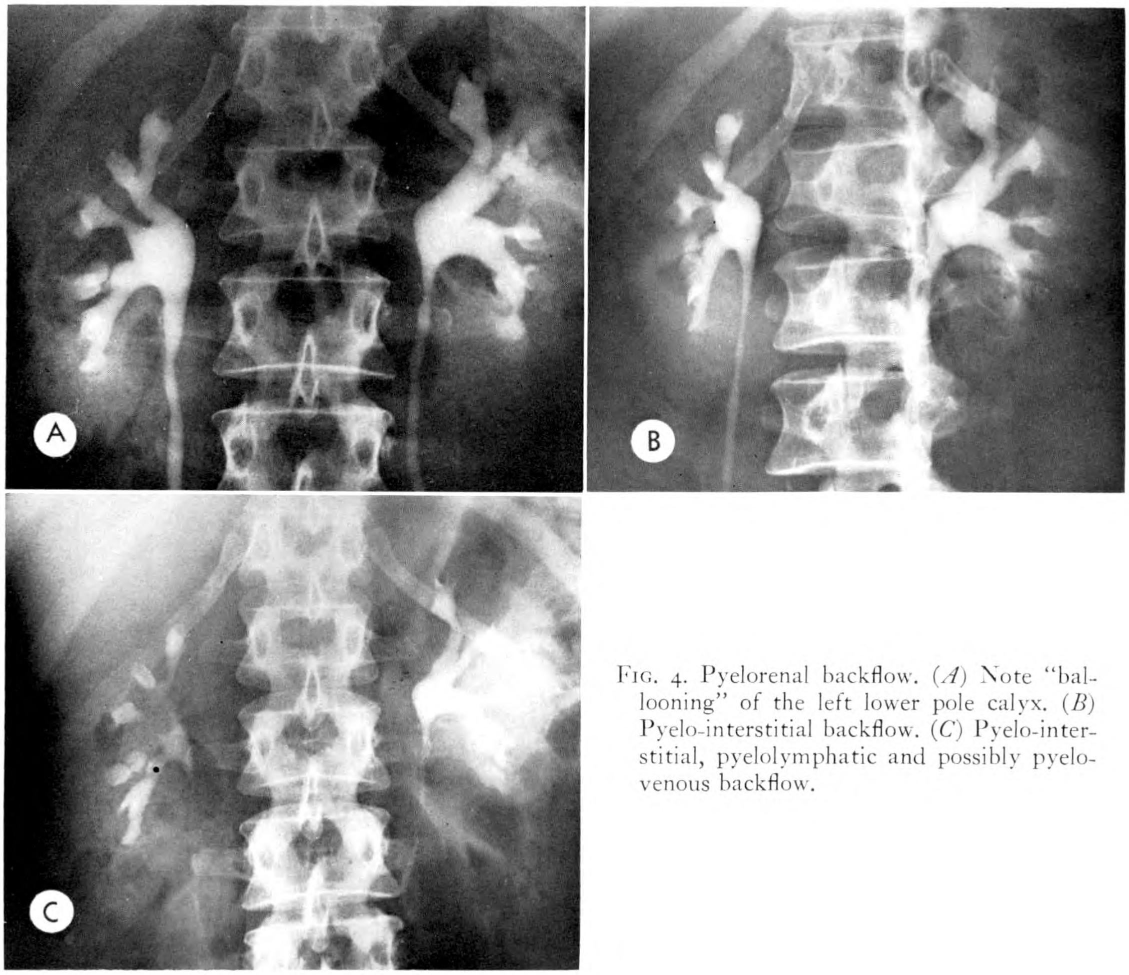

Fig. 4. Pyelorenal backflow. (*A*) Note "ballooning" of the left lower pole calyx. (*B*) Pyelo-interstitial backflow. (*C*) Pyelo-interstitial, pyelolymphatic and possibly pyelovenous backflow.

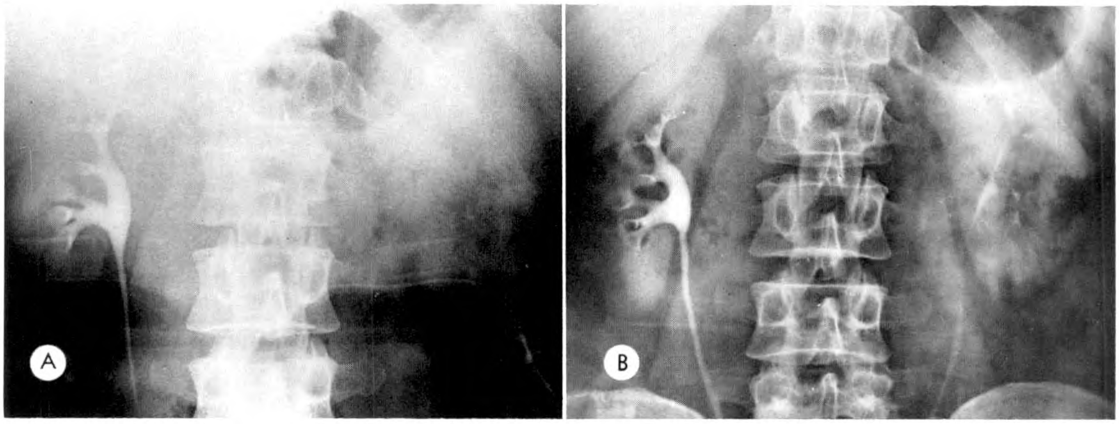

Fig. 5. Anomalous left renal vein. (*A*) In an anteroposterior roentgenogram, a nephrogram but no calyceal filling is seen on the left with compression in place. (*B*) In an anteroposterior roentgenogram following repeat injection of contrast material and without ureteral compression, the left collecting system is visualized.

repeat examination without compression (Fig. 5*B*), however, prompt opacification of the left upper collecting system was observed. At the time of surgical exploration, no abnormal lymph nodes were found but the left renal vein was anomalous, coursing inferiorly and draining into the left common iliac vein. The left renal artery was normal. It was assumed that the anomalous renal vein was occluded by the compression device on the initial examination.

DISCUSSION

Olsson[11] states that "if drainage of the kidney is not obstructed, the renal pelvis and ureter will never be completely filled." We have repeatedly found this incomplete filling of the collecting structures to present a serious problem in evaluation and interpretation of urograms (Fig. 6 through 9). This has resulted in erroneous diagnoses, repeat excretory urograms and unnecessary retrograde pyelograms. Although the incidence is low, there is a potential hazard inherent in all of these examinations. Therefore, it is necessary that the best possible visualization of the anatomy in question be obtained at the time of the initial examination.

The reasons for incomplete filling of the

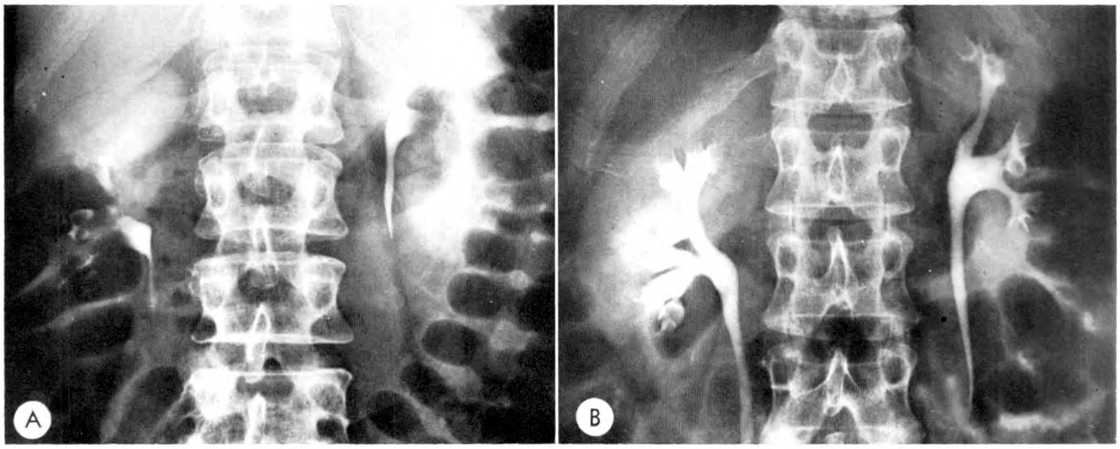

Fig. 6. Normal urograms. (*A*) Incomplete visualization of the pelves and calyces prior to compression. (*B*) After compression, the pelves and calyces are well seen and are normal.

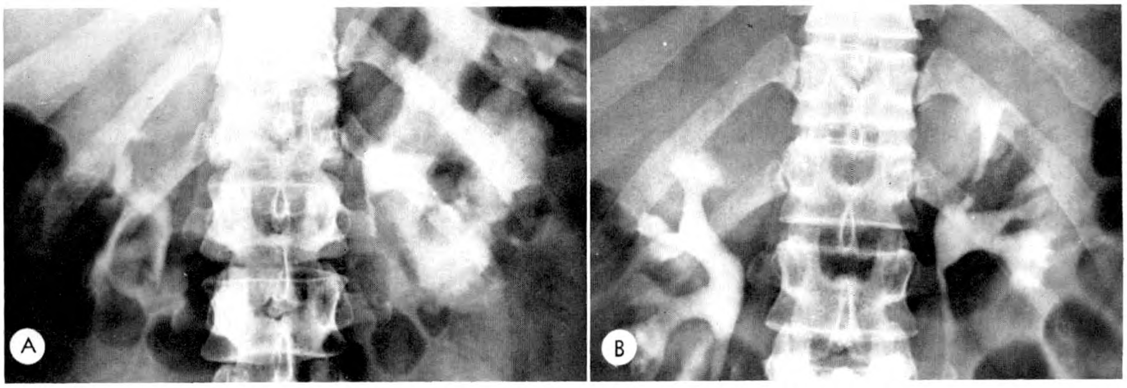

Fig. 7. Normal urograms. (*A*) Incomplete opacification of the pelves and calyces with poor visualization of the left lower pole structures. (*B*) After compression, all calyceal groups are well seen and are normal.

pelvis and calyces in the absence of obstruction are threefold. First, the normal, nonobstructed pelvicalyceal collecting structures and ureters are dynamic organs with periodic peristaltic activity. This systolic and diastolic activity is consistently noted in cinefluorograms and the anatomic details have been well described by Narath.[10] Second, the specific gravity of the opaque media used in excretory urography is such that the opacified urine may layer in the more dependent parts of the collecting system without opacification of the remaining areas. Ettinger[4] has described this as a frequent finding in both excretory and retrograde pyelography. The gross anatomy of the upper urinary tract is the third factor. The superior pole of the kidney is normally more dorsal than the lower pole and the minor calyces are arranged in dorsal and ventral groups relative to the pelvis. Thus, with the patient maintained in the supine position, and without the presence of obstruction, the opacified urine will layer in the more dependent areas of the kidney, leave the upper urinary tract, enter the ureter and pass on to the bladder without opacifying the more ventral parts of the renal pelvis and minor calyces. Pendergrass[12] and later Elkin[2] have recommended the use of additional roentgenograms in the prone position in order to better opacify all parts of the collecting structures. The Trendelenburg and erect positions are also

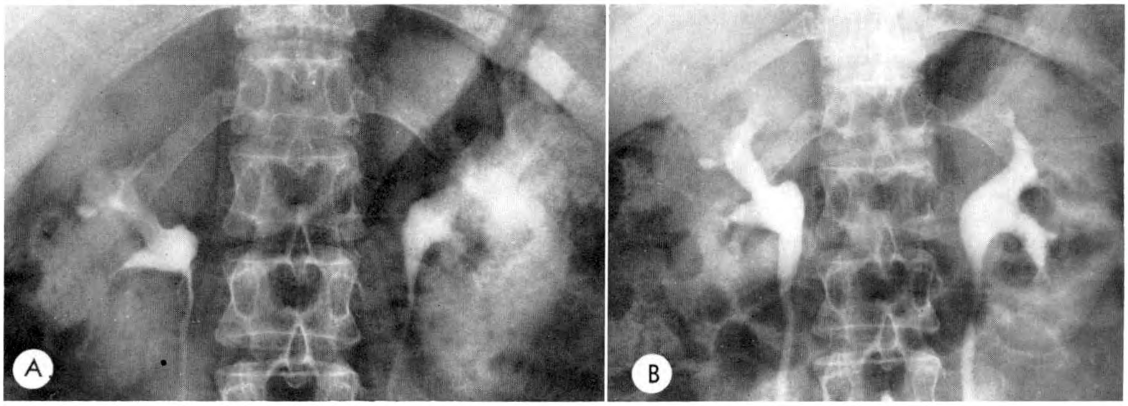

Fig. 8. Calyceal cyst. (*A*) Without compression, the minor calyces are not well seen; a lesion could be present in either lower pole. (*B*) Compression results in excellent filling of the collecting structures bilaterally, revealing the lower pole calyces to be normal. A right upper pole calyceal cyst is present and a partial extrarenal pelvis on the right is now well demonstrated.

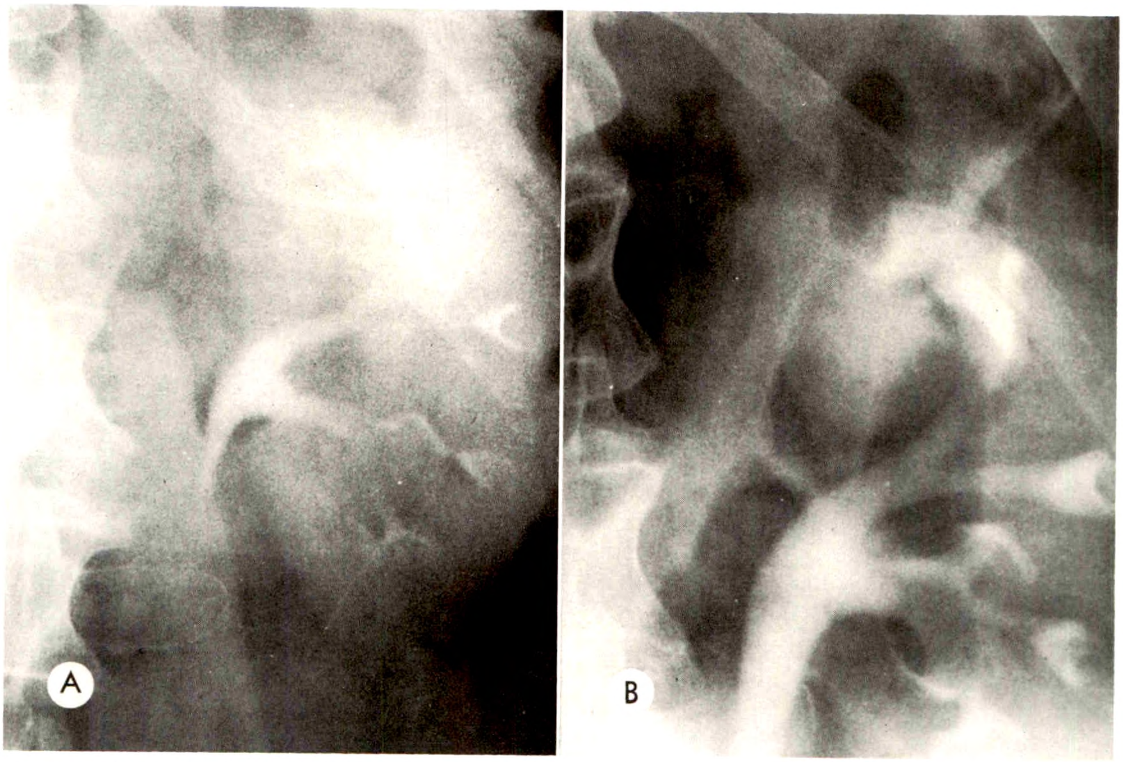

Fig. 9. Multiple renal cysts. (*A*) A roentgengram made without compression suggests extrinsic pressure on the superior pole calyx. (*B*) After compression, two areas of distortion, one in the upper pole and another in the lower peripelvic area, are now well demonstrated.

used by some. However, even with these additional projections, there may be layering of the contrast material and inadequate demonstration of the collecting systems in continuity.

Since urographies are most often performed with the patient in the supine position only, the studies are frequently inadequate, requiring retrograde pyelography for satisfactory anatomic demonstration. With the opaque media available today, proper use of the compression technique can obviate the need for retrograde pyelography in most instances if the kidney is functioning satisfactorily.

Harrow[6,7] has described his compression technique, using a single midline balsa block or rubber bag with a band and rachet attachment on the urographic table for the source of pressure. Heetderks *et al.*[9] describe a similar method using a roll of paper. These are effective methods of compression but limit the examination of the patient to one position because the compression band is attached to the table. This type of compression does not conform to the anatomy of the lower abdomen and produces a disproportionate amount of pressure on the midline structures overlying the lower lumbar vertebral column and sacral promontory. The result is unnecessary discomfort for the patient, unequal compression on the two sides due to a "see-saw" tendency with the vertebral column as the fulcrum and, as mentioned by Harrow and Sloane,[8] lateral displacement of the aorta.

Emmet,[3] and Beare and Wattenberg[1] describe the use of 2 wooden blocks, one over each lower quadrant of the abdomen. This conforms to the regional anatomy but again the patient is limited to one position by the band attached to the roentgenographic table.

The kidneys must be examined in at least 2 different planes for adequate visualization of the pelves and differentiation of the ventral and dorsal minor calyceal groups. This cannot be satisfactorily achieved with the methods described above.

SUMMARY

An efficient and reliable compression device is described which is (1) attached to the patient, (2) permits the patient to move about and (3) conforms to the regional anatomy.

There have been no complications attributable to the use of the device.

With correct use of ureteral compression, complete opacification of the urinary tract is observed with few exceptions and the need for repeat examination or retrograde pyelography is reduced to a minimum.

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URINARY TRACT ANOMALIES IN GONADAL DYSGENESIS[*]

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In 1938 Turner[11] described a clinical entity in phenotypic females characterized by sexual infantilism, congenital webbed neck and cubitus valgus. It has been recognized that a high percentage of these patients had a combination of nonsexual anomalies, including a shield-like chest, micrognathia, high palate, epicanthal folds, low-set ears, hypoplastic nails, idiopathic hypertension, lymphedema of the hands and feet, cutis laxa, keloid formation, mental retardation and deafness.[4]

Subsequently, it was established that approximately 80 per cent of these patients were "chromatin-negative" and lacked the nuclear chromatin-positive body characteristic of genetic females.[10,13] These patients have female external genitalia, uteri and fallopian tubes but no true ovary is present.[12] Chromosomal studies of the "chromatin-negative" patients revealed the presence of 45 chromosomes with an XO sex chromosome constitution.[2] This is in contrast to the normal chromosomal number of 46 with an "XX" sex chromosome complement in normal females and an "XY" sex chromosome complement in normal males. The term gonadal dysgenesis is probably more appropriate than Turner's syndrome because of the wide spectrum of different clinical and chromosomal patterns seen in this entity.[3]

Skeletal abnormalities associated with gonadal dysgenesis have recently been emphasized in the radiologic literature.[1,7,9] The high incidence of abnormal intravenous urograms in this syndrome has not been stressed. Because of the occasional reports of an association of anomalous differentiation of the kidneys and upper urinary tract in gonadal dysgenesis,[5,6,8] all new patients with gonadal dysgenesis seen at this Hospital during the past 2 years have had intravenous urography. The diagnosis of gonadal dysgenesis was definitely established in each phenotypic fe-

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Table I

SUMMARY OF CLINICAL AND ROENTGENOLOGIC FINDINGS

Patient	Age (yr.)	Height (in.)	Height Age (yr.)*	Webbed Neck	Low-Set Ears	Intravenous Urogram
K. W.	2/12	20-3/8	newborn	+	+	Incomplete rotation of right kidney
K. S.	10/12	28-1/4	10/12	+	+	Incomplete rotation of both kidneys
D. F.	2-9/12	32	1-9/12	—	—	Incomplete rotation of right kidney
R. J.	8	42-1/2	5	—	—	Normal
C. R.	10	44-3/4	6	—	—	Incomplete rotation of both kidneys
J. H.	12-4/12	40	8-6/12	—	—	Left ureter-pelvic obstruction with hydronephrosis
B. L.	13-4/12	52-3/4	10	—	—	Horseshoe kidneys
G. P.	13-6/12	58	12	—	—	Left extrarenal pelvis
L. C.	16	56	11-6/12	—	—	Left incomplete rotation; right ureter-pelvic obstruction with hydronephrosis

* From Wilkins, L. The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1957.

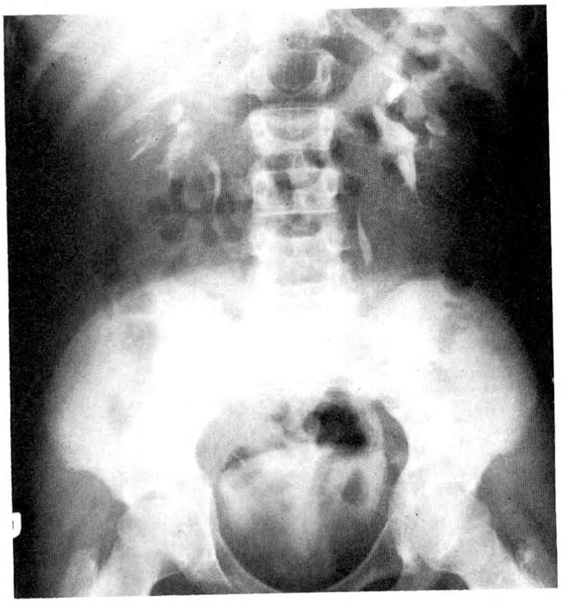

FIG. 1. Patient C.R. Intravenous urogram shows incompletely rotated kidneys.

male by the finding of a chromatin-negative buccal smear and the presence of 45 chromosomes with an XO sex chromosome constitution on chromosomal analysis of leukocytes. The results of intravenous urography in 9 patients are the subject of this report.

ROENTGENOGRAPHIC FINDINGS

In the present series, the over-all incidence of abnormalities seen on intravenous urography is high in comparison to other series. Of 9 patients with gonadal dysgenesis, there were 8 (88.8 per cent) who had abnormal intravenous urograms (Table I). Hortling[5] reported anomalies in 5 of 8 patients (62.5 per cent), while Levin[9] reported that 2 of 3 patients he studied (66.6 per cent) had abnormally rotated kidneys. Jeune and his associates[6] found abnormalities in 16 of 24 patients (66.7 per cent) and Lemli and Smith[8] reported that 9 of 14 patients (64.2 per cent) in their series had anomalies.

Four of our patients had incomplete rotation of one or both kidneys (Fig. 1). Two patients had ureter-pelvic obstruction with hydronephrosis (Fig. 2); 1 had horseshoe kidneys (Fig. 3); and 1 had an extrarenal pelvis on one side. It is interesting to note that the only patient (R.J.) who had a normal intravenous urogram had none of the stigmata commonly associated with gonadal dysgenesis except short stature.

The nature of the abnormalities reported by Jeune *et al.*[6] was as follows: abnormal rotation, 8 cases; horseshoe kidney, 2 cases; low left kidney, 2 cases; unilateral renal hypoplasia, 2 cases; bifid pelvis, 1 case; hydronephrosis, 2 cases; and absence of right pelvis, 1 case.

Lemli and Smith[8] reported the following abnormalities in their 9 patients: horseshoe kidney, 4 cases; unilateral renal agenesis, 2 cases; duplicated renal pelvis, 1 case; bifid collecting system, 1 case; and minor rotational anomaly of the kidneys, 1 case.

The following abnormalities were reported by Hortling:[5] double renal pelvis, 1 patient; double renal pelvis and ureters, 1 patient; abnormal rotation, 1 patient; and horseshoe kidneys, 2 patients.

As seen in Table I, there is no correlation between the presence or absence of webbed neck or low-set ears and the anomalies seen

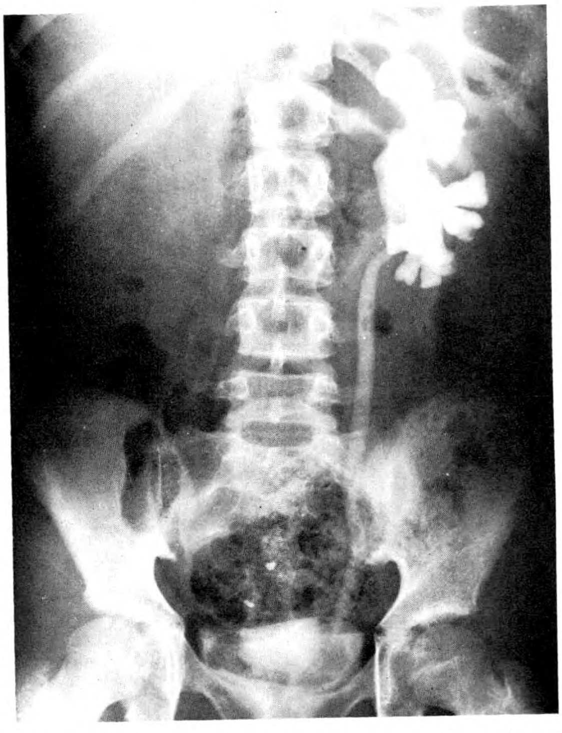

FIG. 2. Patient J.H. Intravenous urogram shows partial ureter-pelvic obstruction with mild hydronephrosis of the left kidney.

on intravenous urograms. Therefore, the presence or absence of any of the commonly occurring stigmata of gonadal dysgenesis cannot be used to predict whether or not abnormalities of the urinary system exist.

Rotational abnormalities of the kidneys are the most common anomaly of the urinary tract seen in gonadal dysgenesis. The great frequency with which anomalies of the urinary tract occur in patients with gonadal dysgenesis suggests that routine intravenous urography is warranted.

SUMMARY

1. Anomalies associated with gonadal dysgenesis as seen on intravenous urograms are more frequent than hitherto reported. In this study of 9 patients, it was found that 8 (88.8 per cent) had some form of urinary tract abnormality.

2. Malrotation of the kidneys was found to be the most frequent renal anomaly in gonadal dysgenesis.

3. Anomalous differentiation of the kidneys and upper urinary tract is sufficiently common in gonadal dysgenesis to warrant routine intravenous urography.

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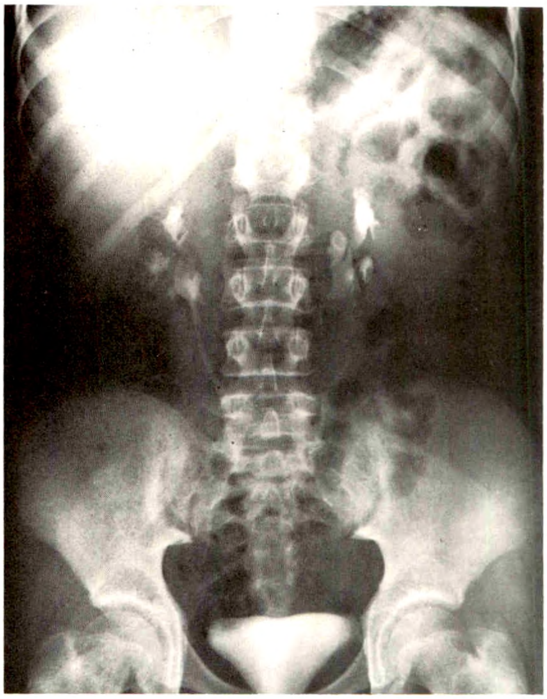

Fig. 3. Patient B.L. Intravenous urogram shows classic horseshoe kidneys.

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URETHROGRAPHIC DIAGNOSIS OF BLADDER NECK CONTRACTION*

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BLADDER neck fibrosis is a common cause of urinary obstruction. Out of 500 cases of bladder neck obstruction treated by open operation, Winsbury-White[6] found bladder neck fibrosis in 31 per cent. At the Lagos University Teaching Hospital, which was opened in August, 1962, out of 37 bladder neck obstructions treated by open operation, 9 were found to be fibrous. The preoperative diagnosis of this common condition is usually difficult and indefinite, being made mainly by a process of elimination of other possible causes of bladder neck obstruction.[6] We here describe a urethrographic sign which may be useful in establishing the diagnosis of bladder neck fibrosis.

MATERIALS AND METHODS

Between February, 1963 and May, 1964, urethrography was carried out at the Lagos University Teaching Hospital on 65 patients who had symptoms and signs of urethral obstruction. These patients were selected for urethrography because they did not have palpably enlarged prostates and their obstruction was presumed to be due to other causes. A large variety of abnormalities was diagnosed with the aid of the urethrograms. These have been described elsewhere.[1] For urethrography, we inject the contrast medium (60 per cent urografin mixed with equal volume of 5 per cent dextran in saline) through a Knutsson's cannula into the urethra, which has been made anesthetic with 2 per cent xylocaine jelly. For the initial part of the examination, the rays are directed sagittally at the root of the penis. First, 20 ml. of the contrast medium is injected to fill the anterior urethra. This is followed by the rapid injection of 10–15 ml., during which the patient is holding his breath and attempting to micturate. The roentgenograms are taken during the rapid injection. Similar rapid injections are made with the patient in both the right and the left semilateral positions, further roentgenograms being taken during all these injections. Lately, we have controlled the injections with fluoroscopic examination with or without image intensification.

When the examination of the urethra has been completed, the bladder is filled with dilute contrast medium and roentgenograms of the bladder are taken. The clamp is then removed and, with the patient standing, oblique roentgenograms of the urethra are taken during micturition.

URETHROVESICAL STREAM EFFECT

In 11 of the 65 patients, during the injection of contrast medium, a jet-like stream effect was noted at the bladder neck (Fig. 1). We have termed this phenomenon the urethrovesical stream effect. Although we have been able to identify it on some roentgenograms published by other workers, we have found no reference to it in the literature.

CLINICAL SIGNIFICANCE OF URETHROVESICAL STREAM EFFECT

On correlating the finding of the urethrovesical stream effect with clinical and operative findings, we have concluded that it occurs in cases of bladder neck contraction. Of the 11 patients whose urethrograms showed the stream effect at the bladder neck, 6 have been treated by open operation; and in all of these the operative diagnosis was bladder neck sclerosis.

One of the remaining 5 patients had linear and regular calcification of the bladder similar to that found in some of the cases of bilharzial bladder neck obstruction described by Fam and Le Golvan[3] (Fig. 2 and 3). In this patient the diagnosis of bladder neck contraction and calcification seems fairly certain, although it has not been confirmed by an open operation. The other 4 patients either refused operation or were too ill for surgery. It appears likely that these are cases of bladder neck contraction, although the diagnosis has not been confirmed.

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Following are case reports of the patients in whom the diagnosis of bladder neck contraction has been confirmed by open operation.

REPORT OF CASES

Case 1. M.N., a male aged 57 years, was admitted on January 28, 1963. He complained of severe difficulty in micturition, a poor stream, diurnal and nocturnal frequency and backache of 6 months' duration. He had a past history of gonorrhea 5 years previously. Physical exami-

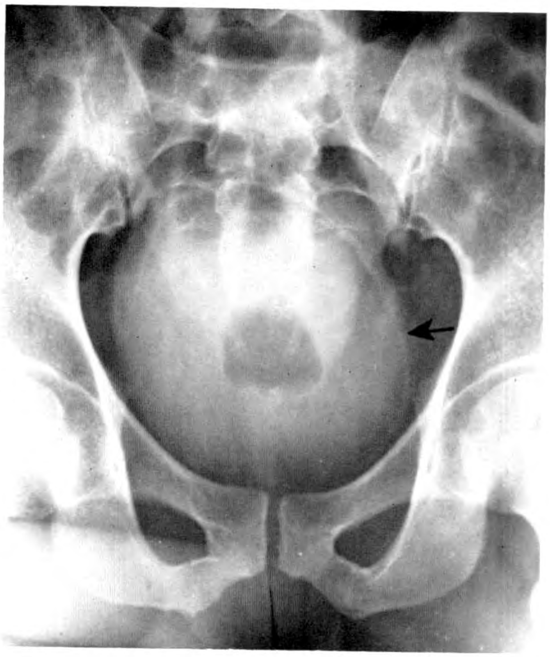

Fig. 2. Plane roentgenogram showing a bladder calcified from old schistosomiasis.

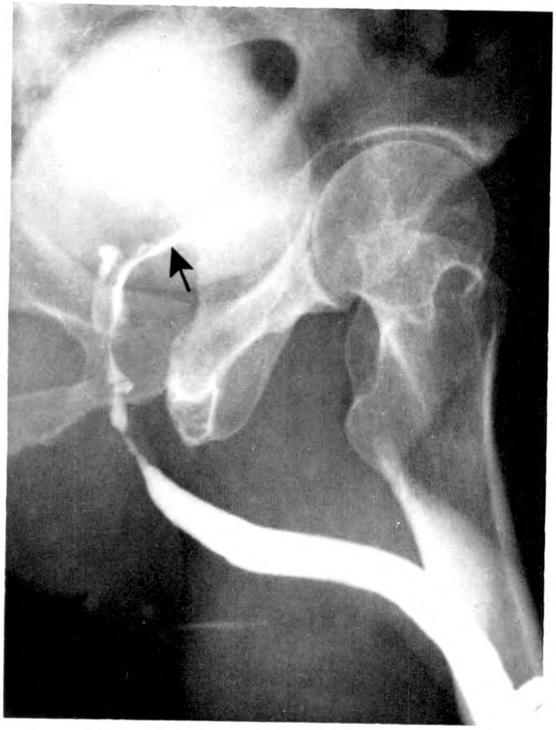

Fig. 1. Arrow points to the urethrovesical stream effect.

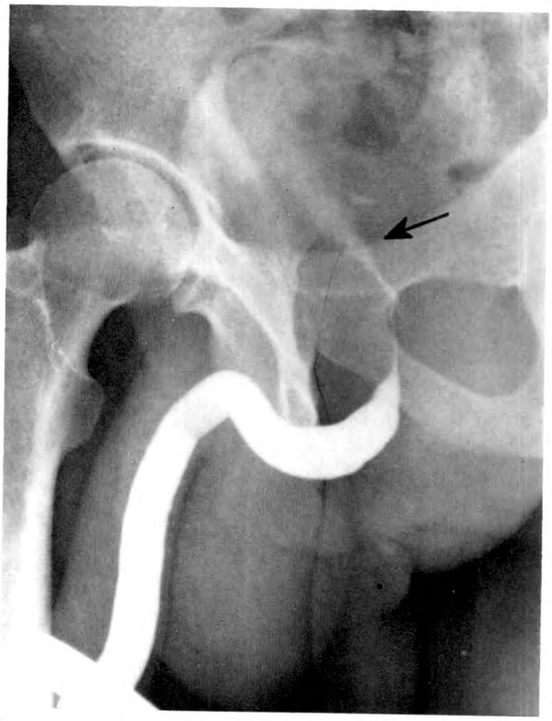

Fig. 3. Arrow points to the urethrovesical stream effect in a patient with a calcified bladder.

nation showed that he had a slightly tender prostate which was not palpably enlarged, a stiff back and a lipoma in his left groin. Hemoglobin was 13.3 gm. per cent and blood urea 62 mg. per 100 ml. Roentgenologic examination of the lumbar spine revealed severe spondylotic changes at the 4–5 level. Urethrograms showed marked irregularity of the proximal part of the carvernous urethra without a definite stricture, and a urethrovesical stream effect. Cystoscopy disclosed marked trabeculation and sacculation of the bladder wall. At operation, bladder neck obstruction by fibrosis was diagnosed and treated by diathermy resection of a wedge from the posterior part of the internal meatus. Postoperative recovery was uneventful and the patient's micturition was improved.

Case ii. O.T., a male aged 34 years, was admitted on June 22, 1963. He complained of frequency of micturition, dribbling, hesitancy and dysuria starting suddenly 1 week before admission. Twelve hours before admission, he developed absolute retention of urine. On examination, his bladder was found to be distended to the umbilicus, but the prostate was not palpable. A No. 10 F. G. Gibbon's urethral catheter was passed easily and the bladder was drained continuously because retention of urine occurred whenever the catheter was withdrawn. Cystoscopy revealed that the mucosa of the base of the bladder was rather hemorrhagic, and urethrograms showed no abnormality other than a urethrovesical stream effect. At operation, bladder neck sclerosis was diagnosed and treated by wedge resection of the posterior lip of the internal meatus. His postoperative recovery was slow but micturition was considerably improved.

Case iii. A. A. M., a male aged 64 years, was admitted on July 28, 1963 because of complete retention of urine for 24 hours. He had had dysuria of fluctuating severity for 16 years and had attended another hospital regularly for urethral dilatation. Physical examination revealed a bladder distended to the level of the umbilicus but no palpable enlargement of the prostate. A Gibbon's urethral catheter was passed easily and the bladder was drained continuously. Hemoglobin was 14.0 gm. per cent and blood urea was 23 mg. per 100 ml. Cystoscopy revealed marked trabeculation and sacculation of the bladder wall. At operation, bladder neck fibrosis was diagnosed and treated by wedge resection of the posterior part of the internal meatus. Following this, he could pass urine well.

Five months after operation the patient complained of return of dysuria and a poor stream. Urethrography done at this time showed filling of the prostatic ducts with contrast medium as well as the urethrovesical stream effect. It is presumed that the contraction of the bladder neck has recurred.

Case iv. H. S., a male aged 57 years, was admitted on February 27, 1964 with a history of dysuria, poor stream and dribbling for 6 months. On examination, his bladder was distended and his prostate was rather firm and only slightly enlarged. Two days after admission he developed absolute retention of urine. A No. 10 F. G. Gibbon's catheter was passed easily and his bladder was drained continuously. Hemoglobin was 12.1 gm. per cent and blood urea 72 mg. per 100 ml. Urethrography revealed a urethrovesical stream effect and irregularity of the proximal part of the cavernous urethra without a definite stricture but with some intravasation of contrast medium into the corpus spongiosum. At operation, the diagnosis of bladder neck obstruction by a small fibrous prostate was made and a wedge resection was performed. He recovered well, though slowly, from the operation.

Case v. M.A., a male aged 68 years, was admitted on March 3, 1964 with a history of absolute retention of urine for 36 hours. This had come on suddenly and there was no previous history of dysuria or frequency. On examination, the bladder was distended nearly up to the umbilicus, and the prostate felt knobby, but was only slightly enlarged. A Gibbon's urethral catheter was passed and the bladder drained. Hemoglobin was 13.7 gm. per cent and blood urea was 42 mg. per 100 ml. At operation, the diagnosis was made of prostatic fibrosis and bladder neck contraction. A circular rim of tissue, including prostatic tissue, was removed with the diathermy. The patient made an uneventful recovery and his micturition was practically back to normal.

Case vi. A.A., a male aged 40 years, was admitted on December 2, 1963. He complained of severe dysuria, dribbling, poor stream and frequency of micturition, all of which had been present for a long but rather indefinite time and had worsened in the 6 days preceding admission. The patient was obviously ill. The bladder was not easily palpable and the prostate was not enlarged. Hemoglobin was 10 gm. per cent and blood urea was 79 mg. per 100 ml. A plain roentgenogram of the pelvis revealed a small calcified bladder and an intravenous pyelogram showed that the left kidney was not functioning and the right kidney was grossly hydronephrotic. Urethrography showed a urethrovesical stream effect. Although no ova of *Schistosoma* were found in the urine, the calcification of the bladder was presumed to be due to old schistosomiasis. Suprapubic cystostomy was performed to establish better drainage of the bladder. At operation, the bladder was found to be small and rigid, and the internal meatus was pin-holed from sclerosis and calcification of the bladder neck. The patient rapidly deteriorated and died from renal failure.

EXPERIMENTAL EVIDENCE OF THE SIGNIFICANCE OF URETHROVESICAL STREAM EFFECT

We have attempted to evaluate the clinical significance of the urethrovesical stream effect by a simple experiment. For this we used a bladder-urethra equivalent, made from a toy rubber balloon and a piece of rubber tubing which had an internal diameter of 1.5 cm. (Fig. 4). The balloon was filled with 200 ml. of water.

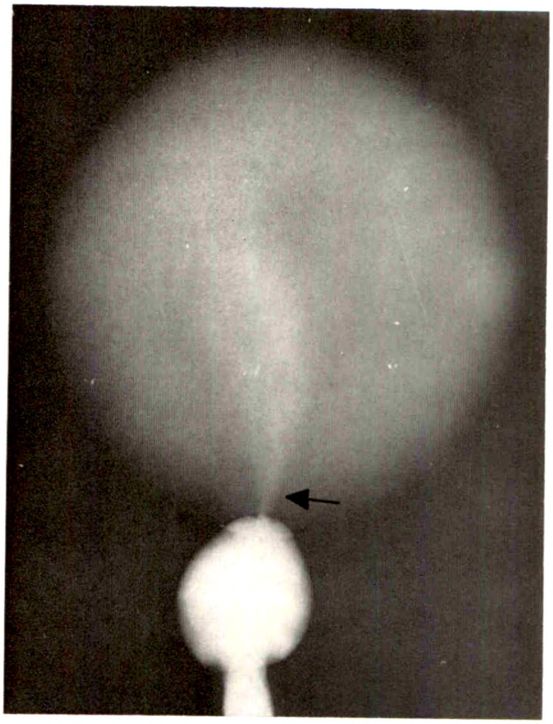

Fig. 5. Arrow points to the "urethrovesical" stream effect produced by constricting the neck of the balloon with a string.

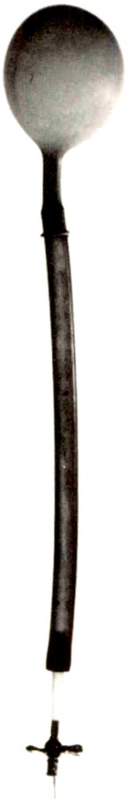

Fig. 4. Bladder-urethra equivalent.

When the neck of the balloon was constricted by a string, a jet-like stream effect was produced on injecting the contrast medium (Fig. 5). On removing the constriction from the neck of the balloon, no stream effect was produced. The laminar structure of the stream effect was replaced by a turbulent type of flow (Fig. 6).

DISCUSSION

Lindblom *et al.*[5] state that the urethrocystographic sign of bladder neck contraction is a barrier protuding from behind and to which the alternative name of posterior bar may be given. Bladder neck fibrosis occurs mainly in 2 forms, *i.e.*, the

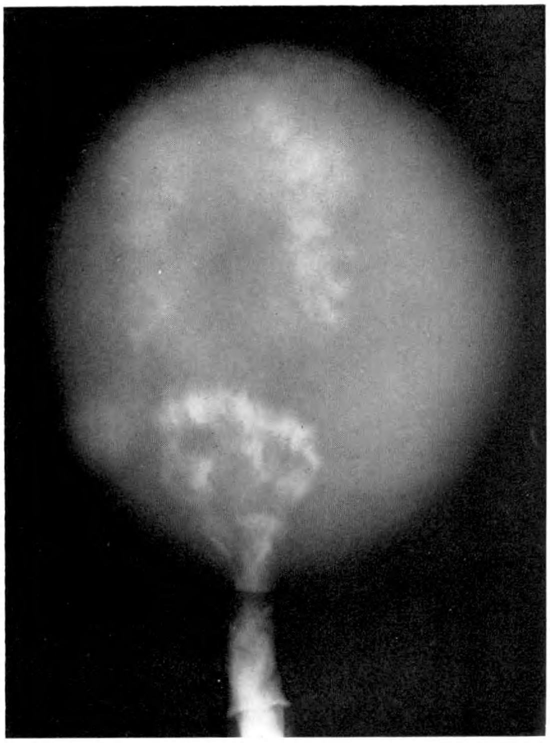

Fig. 6. There is no stream effect when the neck of the balloon is not constricted.

circular type in which the fibrosis involves equally the whole circumference of the internal meatus, and the posterior (or median) bar type in which there is an elevation of the posterior lip. Irwin[4] found that two-thirds of 48 cases of bladder neck fibrosis treated by open operation fell into the circular group, while only one-third fell into the posterior bar group. The urethrocystographic sign described by Lindblom *et al.*[5] refers only to the latter type. The sign which we have described here is particularly useful in the diagnosis of the much more common form of bladder neck fibrosis—the circular type. Emmett[2] describes a sign of bladder neck contraction on retrograde urethrograms produced by the injection of viscous contrast medium. As the medium is forced through the narrowed opening at the bladder neck, it "layers out" in the bladder much as toothpaste extruded from a tube. The same physical arrangement which produces this "toothpaste sign," gives the "stream effect" with a more fluid medium.

SUMMARY

1. A jet-like stream effect has been noticed to occur at the bladder neck in some patients during the injection of the contrast medium for retrograde urethrography. This phenomenon is termed the "urethrovesical stream effect."

2. Clinical and experimental evidence is presented to show that the urethrovesical stream effect is a sign of bladder neck contraction.

3. This urethrographic sign is, therefore, offered as an aid to the preoperative diagnosis of bladder neck contraction.

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CALCIFICATION IN URINARY BLADDER TUMORS

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IN THE past several years, there has been much written concerning the roentgenographic demonstration of calcifications in primary and secondary tumor masses.[2–5] While in many cases, pathologic examination reveals calcification in the necrotic tumor, the recognition on plain roentgenograms is less common. An excellent review of abdominal calcifications has been presented by McAfee and Donner.[4] They re-emphasized the occasional presence of calcium in urinary bladder tumors. Emmett[1] in his textbook of urology also shows examples of calcification in urinary bladder tumors. Because of the rather low incidence of such observations, we felt it worthwhile to report our series of cases with specific regard to the type of calcification demonstrated roentgenographically.

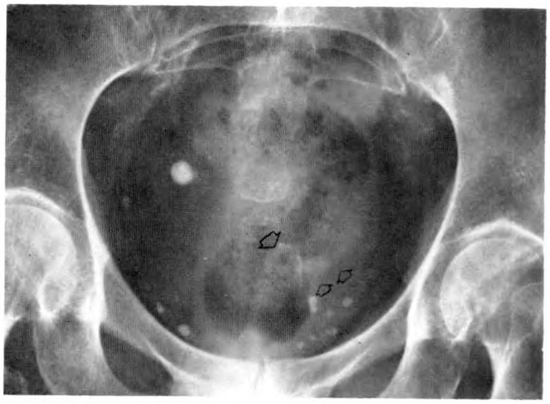

FIG. 1. Plain roentgenogram of the pelvis shows a homogeneously calcific density with a fine denser rim (single arrow). Adjacent to this is noted speckled calcification (double arrows). This case demonstrated two types of calcification in a urinary bladder tumor.

MATERIAL AND CLASSIFICATION

Five cases of calcified bladder tumors were noted in 75 cases of urinary bladder tumors examined. One case, interestingly enough, demonstrated two different types of calcification.

Generally, three types of calcification were seen in the 5 positive cases: (1) hazy calcification, well circumscribed with a dense rim simulating the appearance of a bladder stone. Close inspection with a hand lens failed to show any lamellar structure (Fig. 1, 2, 3 and 4); (2) fine speckled calcifications, arranged irregularly or serpiginously with no definite margin (Fig. 1, 2, 3 and 4); and (3) coarse nodular calcifications with an ill-defined margin (Fig. 5).

Of the five tumors noted, one multifocal case (Fig. 1, 2, 3 and 4) demonstrated both Type 1 and Type 2 calcification. Three cases were seen with the Type 2 variety. One case, as demonstrated in Figure 5, showed the calcification of Type 3. Four of the 5 cases were transitional cell carcinomas. The single calcified squamous cell carcinoma showed the serpiginous calcification of Type 2. In this particular case, it was felt that an element of encrusted calcified cystitis was also present, but the tumor did contain within its substance small areas of calcific deposition.

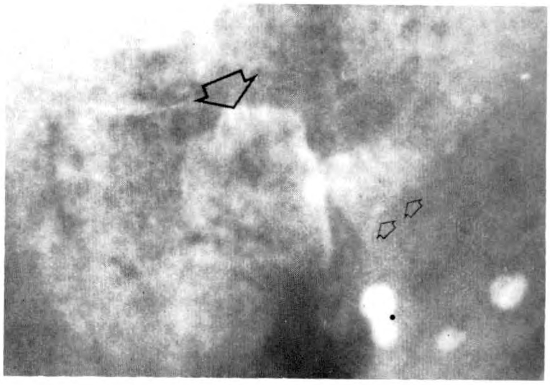

FIG. 2. Magnified view of Figure 1 shows the calcifications to better advantage.

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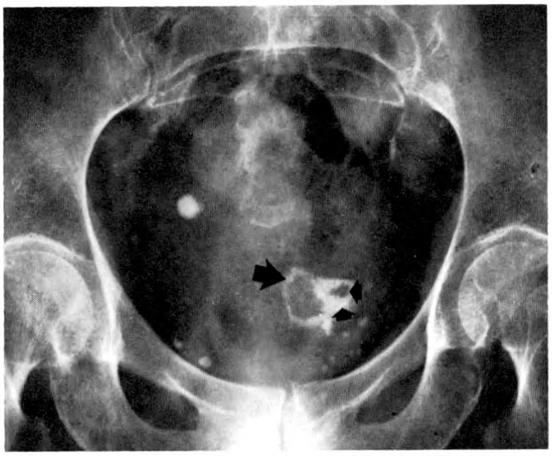

FIG. 3. Intravenous pyelogram of same case as in Figures 1 and 2 showing two contiguous bladder tumors (filling defects indicated by arrows) coated with opaque material.

COMMENT

Calcifications within the bladder or its wall do occur quite often. Among these, calculi are the most common and could conceivably be mistaken for a bladder tumor with calcification. The converse, however, would be more likely. Bladder stones are ovoid in shape with a homogeneous density, and cartwheel or annular appearance. They may be mobile, although impaction does occur.

Encrusted cystitis can on occasion calcify, and tends toward speckled calcifications. Serpiginous calcifications as in bladder tumors may also be seen.

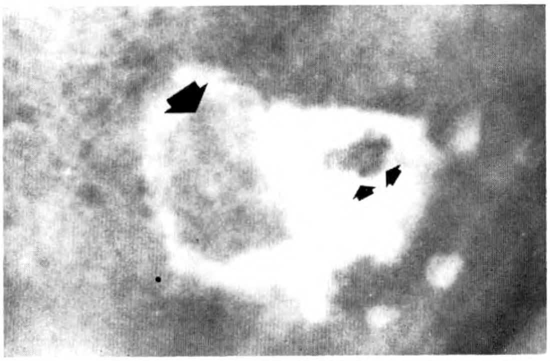

FIG. 4. Magnified view of Figure 3. The shape of the two filling defects noted on positive contrast study here conforms to the configuration and location of the calcifications noted in Figures 1 and 2.

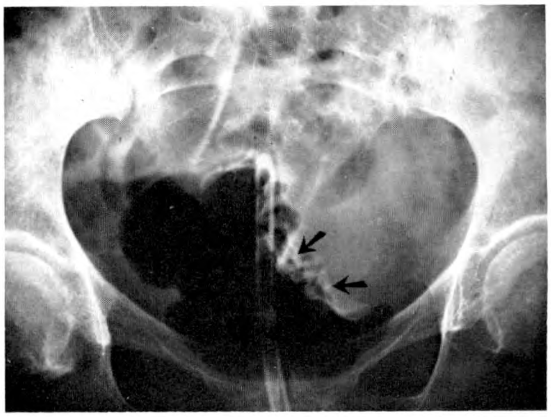

FIG. 5. Air contrast study of infiltrating urinary bladder tumor demonstrating the nodular calcifications in the tumor.

Tuberculosis may result in small or large collections of calcium within the lumen itself. There is frequently associated ureteral and renal calcification as well. Arc-like calcifications of the bladder wall, similar to schistosomiasis, have also been noted.

Schistosomiasis, not infrequently, presents bladder wall calcification in the form of a "cast" of the bladder and the lower ureters may likewise be calcified.

Retained foreign bodies such as a sponge, Foley catheter, and blood clots may calcify. One would expect the type of calcification in these instances to depend on the shape of the retained foreign body.

Unusual cases of calcification include echinococcus, hemangioma, neuroblastoma and other less common tumors.

CONCLUSION

In evaluating the findings on plain roentgenograms in carcinoma of the urinary bladder, careful scrutiny of the pelvis may reveal calcification in the tumor. While the types of calcifications we encountered were not of pathognomonic significance, we feel that awareness of their presence is of aid in the diagnosis of urinary bladder tumors. Of course, cystoscopic examination remains the most accurate method of diagnosing bladder tumors. Opaque material or air cystography is of considerable value for estimating the intraluminal extension and the extent, if any, of involvement of the bladder musculature. Arteriography can be of value in determining the degree of involvement of the bladder wall musculature as well as of the perivesical infiltration. All these clinical and roentgenographic contrast studies are usually performed in the face of suspicious clinical symptoms.

The patients we have seen with calcification in urinary bladder tumors were all symptomatic; however, we feel, that by particular attention to the scout roentgenograms of asymptomatic patients, one could find a valuable clue in the diagnosis of bladder tumors by noting calcifications of the described types.

SUMMARY

Five cases of calcified urinary bladder tumors have been noted in 75 cases examined.

Three types of calcifications were seen: (1) hazy opacity with a dense rim; (2) speckled irregular or serpiginous stippling; and (3) nodular, coarse calcification.

It is suggested that evaluation of the plain roentgenogram may, on occasion, yield a clue to the diagnosis of urinary bladder tumors. Awareness of the significance of the calcification of the described types should lead to more definitive procedures.

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ROENTGENOLOGICALLY DEMONSTRABLE CALCIFICATION IN TUMORS OF THE BLADDER*

REPORT OF THREE CASES

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CALCIUM as a roentgenographic manifestation of tumors of the urinary bladder is an uncommon finding. Emmett[3] stated that urinary salts may be deposited on the surface of any type of urinary neoplasm and that calcification often occurs in tumor necrosis. Nevertheless, in a series of 1,000 cases of proven bladder tumors, of which 732 had roentgenographic examinations, Braband[1] found only 5 (0.69 per cent) that contained roentgenographically demonstrable tumor calcification. This was in contrast to the more commonly noted findings of filling defect in the bladder (36.8 per cent), hydronephrosis or hydroureter (9.8 per cent), unilateral functionless kidneys (9.01 per cent), and filling defect in the bladder plus upper urinary tract changes (6.4 per cent).

Interest in this subject was stimulated by the finding of 3 cases at our clinic in which calcific densities, which were unlike the usual densities of phleboliths, uterine fibroids, or vesical stones, were seen on roentgenograms of the pelvis. These densities were subsequently shown, by appropriate contrast studies, to be located within filling defects in the urinary bladders of the 3 patients, and the ultimate pathologic diagnosis in each case was malignant tumor.

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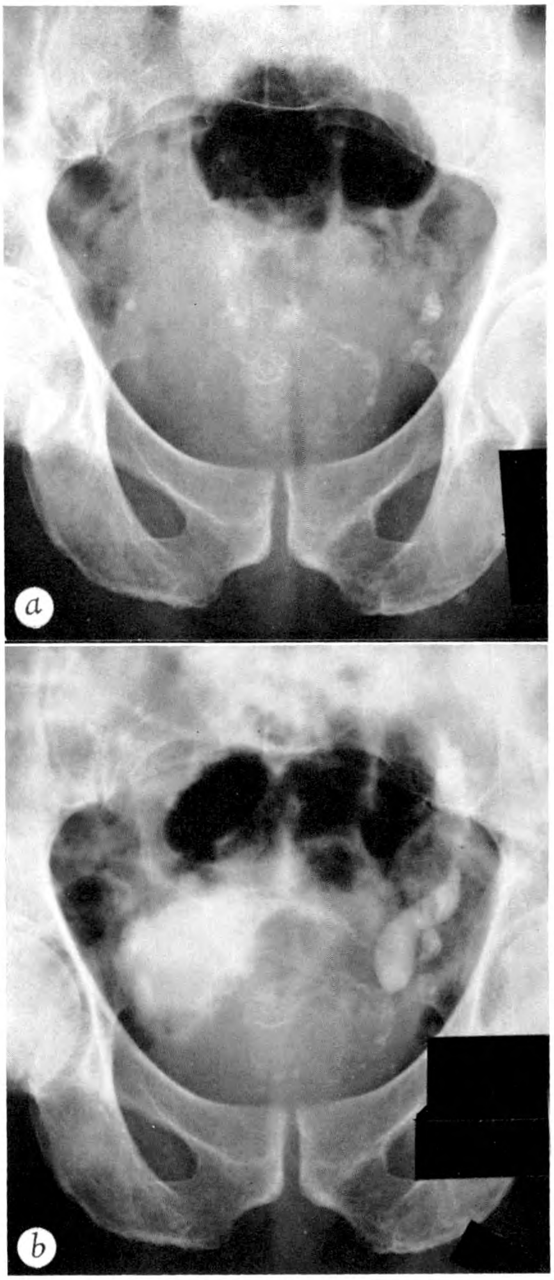

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FIG. 1. Case 1. (*a*) Irregular calcific density in region of urinary bladder. (*b*) Calcium deposits within large tumor in lower and left lateral portions of urinary bladder.

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REPORT OF CASES

CASE I. A 75 year old white man had had a diagnosis of chronic lymphocytic leukemia in 1956. He was doing very well, however, when seen January 22, 1963. On June 12, 1963, he presented with gross hematuria of 11 days' duration. This subsequently became associated with increased urinary frequency and an increase of nocturia from 1 to 5 times per night.

Physical examination revealed a chronically ill appearing white man with slight splenomegaly, small right axillary lymph nodes, and a slightly enlarged, benign-feeling prostate. Calcium was identified in the left region of the pelvis (Fig. 1*a*), and an excretory urogram revealed a large, partially-calcified, space-occupying lesion in the left side of the bladder with some dilatation of the lower portion of the left ureter (Fig. 1*b*). With the patient under general anesthesia, a transurethral resection of the vesical lesion was performed. The histologic diagnosis was papillary transitional cell carcinoma of the bladder (Fig. 2).

CASE II. A 54 year old white man presented at the Mayo Clinic on February 9, 1962, with nocturia, frequency, dribbling, hesitancy, narrowed stream, and a history of numerous transurethral resections that had been done for urinary retention during the preceding 3 years.

On physical examination, he was found to have a firm, irregular, and slightly enlarged prostate. A roentgenogram of the abdomen revealed calcium in the region of the trigone (Fig. 3*a*), and a cystogram demonstrated an associated filling defect of the urinary bladder (Fig. 3*b*). A transurethral resection was performed, and carcinosarcoma, containing elements of osteogenic sarcoma, was the pathologic diagnosis (Fig. 4).

CASE III. This 72 year old white man presented at the Mayo Clinic in 1954 with signs and symptoms of urinary obstruction. A transurethral resection was done, and the pathologic diagnosis was benign prostatic hypertrophy. For 9 years he was well, and did not return until September 17, 1963, at which time he presented with painless gross hematuria that was intermittent during the preceding 2 months; he had noted some mild frequency and nocturia. Physical examination revealed a blood pressure of 210 mm. of mercury systolic and 110 mm. diastolic, a hard pulsating mass in the left upper quadrant of the abdomen, and eyeground changes of group 3 hypertension (Keith-Wagener-Barker grouping). Blood urea nitrogen was 57 mg. per 100 ml., and a roentgenogram of the abdomen revealed calcium deposits in the right side of the pelvis in the region of the urinary bladder (Fig. 5). A cystogram showed marked deformity of the bladder. At laparotomy, two significant lesions were found: a very large aortic aneurysm, and a 6 by 8 cm. ovoid mass on the right inferior aspect of the urinary bladder. A biopsy of the ovoid mass indicated a leiomyosarcoma (Fig. 6).

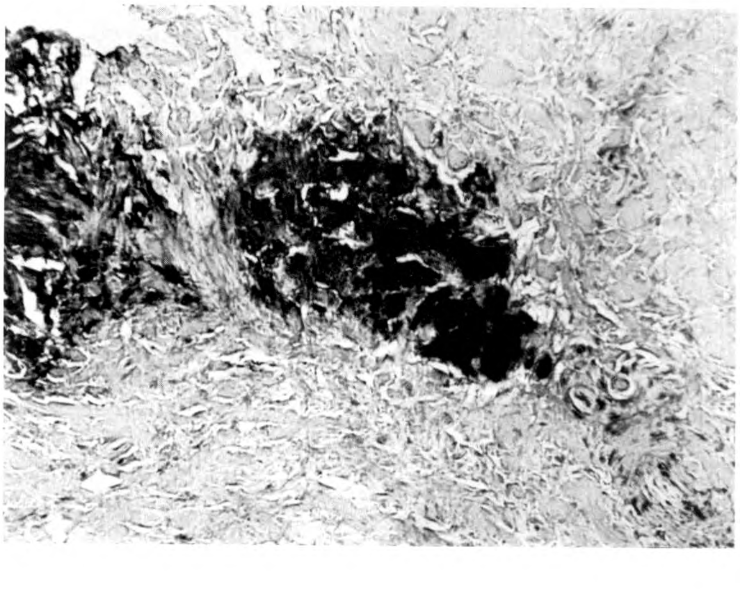

FIG. 2. Case I. Collection of calcium in area of tumor necrosis (hematoxylin and eosin; ×175).

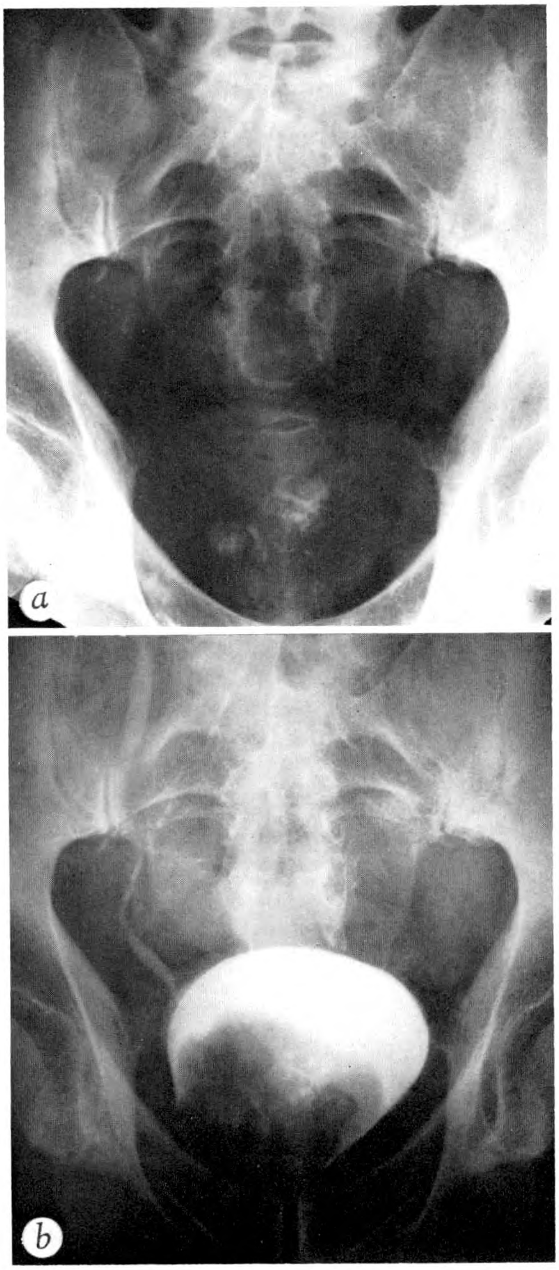

FIG. 3. Case 11. (*a*) Amorphous calcification in mid-urinary bladder region. (*b*) Calcification within lobular mass lesion of right lower urinary bladder.

MATERIALS AND METHODS

In each case, slides from the original biopsy specimen were reviewed for confirmation of diagnosis and for evidence of calcification within the tumor; no calcium was seen. Of the three gross specimens obtained at operations, only two (Cases 1 and 11) were available for review. Roentgenograms were made of these, and calcific densities were found and localized in both specimens. With these roentgenograms as guides, appropriate sections were stained with hematoxylin and eosin and demonstrated calcium deposits. The calcific nature of these deposits was confirmed with the use of the von Kossa stain.

DISCUSSION

Hilbish and Bartter[4] grouped abnormal calcium deposits in soft tissue into 6 general categories: (1) metastatic calcification as occurs in renal tubules and other regions in the event of increased serum calcium, increased tissue alkalinity, or hyperphosphatemia; (2) calcinosis, as seen in dermatomyositis and scleroderma; (3) dystrophic calcification, the most common type, which occurs in devitalized tissue, necrotic neoplastic tissue, etc.; (4) heterotopic bone formation, as in myositis ossificans; (5) vascular calcification; and (6) stone formation, as occurs in kidney and gallbladder.

A slide was prepared from the calcium-containing specimen of Case 1, the transitional cell carcinoma. It exhibited a rather disarrayed collection of crystalline-like material within a framework of pyknotic nuclei and definitely necrotic tissue—all features of dystrophic calcification (Fig. 2).

Pang,[7] in reviewing the world literature concerning primary bony and cartilaginous tumors of the urinary bladder in 1958, found reports of 15 such cases, and he presented 5 additional ones. Lesions in these cases were classified as follows: (1) mixed mesenchymal and epithelial tumors (7 cases); (2) primary osteosarcoma and chondrosarcoma (11 cases); and (3) epithelial tumors of the bladder with stromal osseous metaplasia (2 cases). Although there was no mention of roentgenographically demonstrable calcification in these tumors, calcium or actual bone was noted histologically in 16 of the 20 cases, and the histologic identification of densely calcified bone trabeculae was stressed in 3 cases.

In 1959, Nicolai and Spjut[6] described a

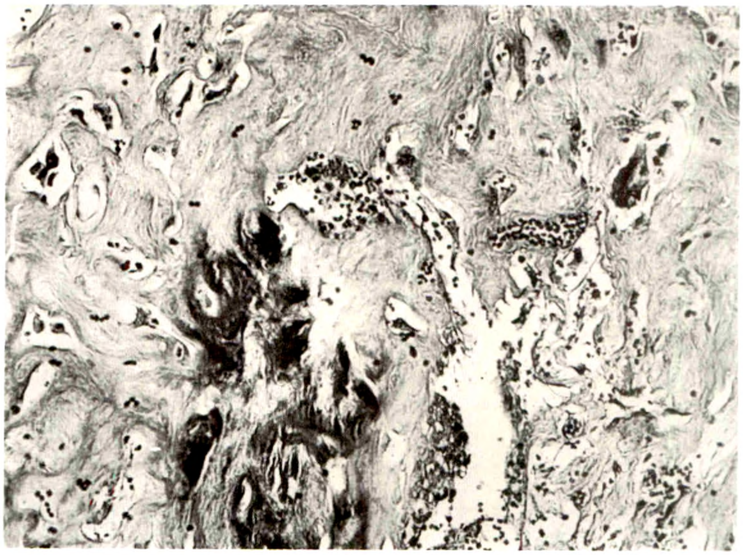

FIG. 4. Case II. Area of osteoid formation within malignant stroma (hematoxylin and eosin; ×160).

case involving primary osteogenic sarcoma of the urinary bladder, but there was no report of calcification seen roentgenographically within the lesion. Dahlin[2] said, "To qualify in this category (as osteosarcoma) the proliferating malignant cells of the neoplasm must produce osteoid substance or material histologically indistinguishable from it in at least small foci." Although the histology of these lesions is extremely variable, Lichtenstein[5] stated that 2 criteria are necessary for this diagnosis: (1) the presence of frankly sarcomatous stroma and (2) direct formation of tumor osteoid and bone by this malignant connective tissue. Mineralized osteoid in a degenerating portion of the sarcomatous elements was seen in our Case II (Fig. 4).

As previously noted, the necrotic tissue that surrounds the calcium deposits in Case I categorizes this lesion as dystrophic calcification, the third group of Hilbish and Bartter.[4] The osteogenic sarcoma of Case II can be classified reasonably as heterotopic bone formation, group 4. Although histologic demonstration of the calcium seen roentgenographically in Case III was not possible, since the gross specimen was not available, it too probably represents dystrophic calcification.[3]

The roentgenographic appearance of the calcification in these 3 cases is described best as amorphous in nature and diffuse in distribution. As such, the lesions are readily distinguished from the calcification of urinary bladder stones, the curvilinear calcification that occurs in bladder diverticula or the chronically infected urinary

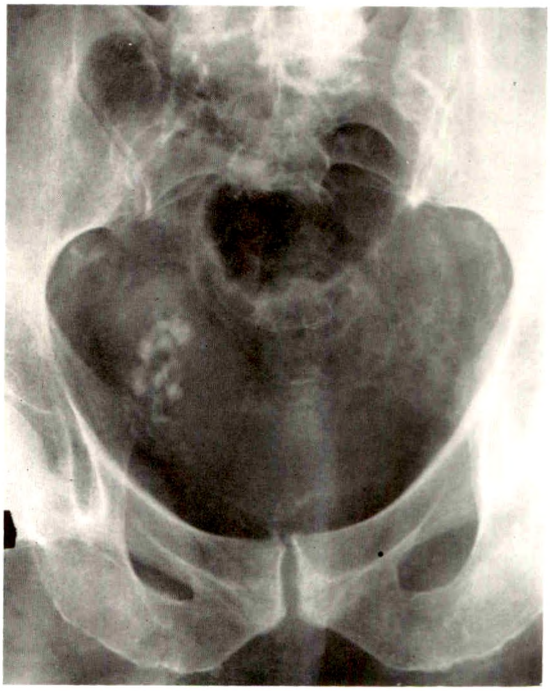

FIG. 5. Case III. Mottled calcific density in right lateral pelvis.

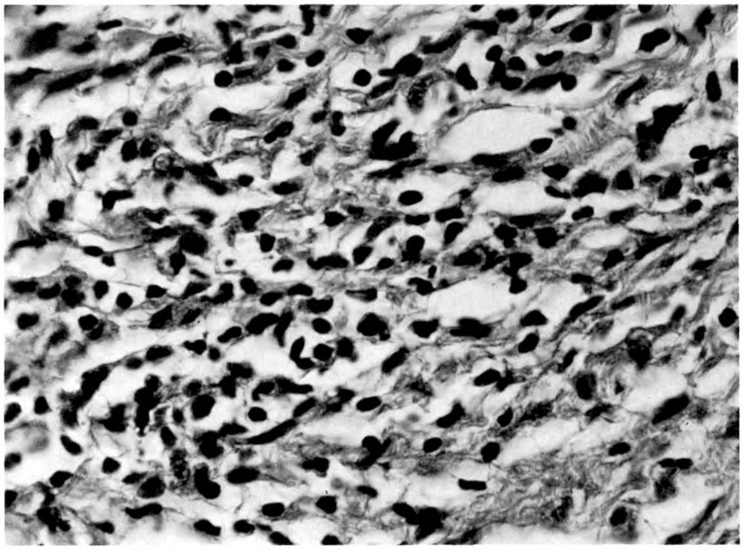

FIG. 6. Case III. Leiomyosarcoma of urinary bladder; apparent clefts are artifactual (hematoxylin and eosin; ×500).

bladder, and the calcification seen as an incidental finding in the region of the prostate.

SUMMARY

The literature with regard to roentgenologically demonstrable calcification of urinary bladder tumors has been surveyed, and 3 additional cases in which this phenomenon occurred have been reported. The extremely rare finding of a primary osteogenic sarcoma of the urinary bladder and a brief review of the related literature have been presented. The finding of unusual calcific densities in the region of the urinary bladder within a space-occupying lesion probably is an ominous sign.

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All slides were reviewed with the assistance of Drs. David Dahlin and E. G. Harrison, Jr., of the Mayo Clinic Section of Surgical Pathology.

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ARTERIOGRAPHIC STUDY OF RHABDOMYOSARCOMA OF THE URINARY BLADDER*

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RHABDOMYOSARCOMA (sarcoma botryoides), though relatively rare, is one of the major urogenital tumors of childhood.[2] Because of its sarcomatous origin, this tumor tends to extend locally before metastasizing distantly. Complete surgical removal and resultant cure are possible if the extent of the tumor and its major blood supply can be determined. Arteriography can provide such information.

The tumor vascular patterns of sarcoma botryoides are presented in this report. In addition, the pertinent clinical, cystoscopic and operative findings are documented.

REPORT OF A CASE

A 5 year old white male was referred to the University of Missouri Medical Center following 2 weeks of frequency, dysuria, urgency and strangury. The child had been treated with antibacterial agents for what was considered to be a cystitis. When symptoms persisted and a lower abdominal mass appeared, catheterization was attempted for the supposed urinary tract retention. Since the suprapubic mass did not disappear, an impassable obstruction was assumed.

On admission, catheterization revealed no retention of urine and the urinalysis was within normal limits. A bimanual rectal-abdominal palpation revealed a large, firm, suprapubic mass which was thought to be of vesical origin. Though the mass was movable, it completely filled the pelvis; and therefore it was not possible to determine whether any infiltration of contiguous structures had occurred.

A retrograde cystogram demonstrated displacement of the urinary bladder to the right, anteriorly, and superiorly by a massive tumor arising either in the urinary bladder wall or adjacent to the bladder (Fig. 1*A*). The bladder mucosa appeared intact and there were no intravesical filling defects. Excretory urograms showed delayed opacification of a hydronephrotic left upper urinary tract and relative normalcy of the right upper urinary tract (Fig. 1*B*). The chest roentgenogram was normal.

At cystoscopy a smooth surfaced vesical wall mass was seen projecting from the left lateral and posterior aspects of the bladder. The characteristic grape-like clusters of a true botryoid type of sarcoma were not visible. Biopsies were taken and reported as consistent with sarcoma. Subsequent histologic examination revealed the presence of rhabdomyosarcomatous elements. At the conclusion of the endoscopic procedure, anesthesia was maintained and arteriography was performed.

Using the Seldinger technique,[1] a 40 cm. red Ödman catheter with side holes was passed from the right common femoral artery into the distal aorta. Thirty cubic centimeters of methylglucamine diatrizoate* was injected under 8 kg. per square centimeter pressure by a Gidlund injector. Roentgenograms were obtained at the rate of 2 per second for 5 seconds and 1 per second for 7 seconds. Tourniquets were applied to the mid-thighs bilaterally just prior to injection.

The arteriogram demonstrated a large single tumor mass confined to the pelvis. Extension to bone or other adjacent structures was not depicted. The main tumor blood supply was from the vesical and middle hemorrhoidal branches of the hypogastric arteries, particularly the left (Fig. 2*A*). The tumor vessels were tortuous and irregular in caliber, and were diffusely spread throughout the pelvis (Fig. 2*B*). Later studies showed early venous filling and venous laking (Fig. 2*C*).

At surgery, the bulk of the tumor mass and the close confines of the bony pelvis made cystectomy somewhat difficult. The prior knowledge of the location of the main arterial blood supply reduced blood loss to a negligible point. The urinary bladder and tumor were removed. There was no evidence of involvement of contiguous structures or adjacent lymph nodes. More distant metastases were not apparent. The urine was diverted by ureterosigmoidostomy.

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* Renografin-60, E. R. Squibb & Son, New York.

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Histopathologic examination of the tumor not only confirmed the rhabdomyosarcomatous nature of the neoplasm but the absence of regional lymph node involvement as well.

DISCUSSION

Malignant neoplasms of the urinary bladder in children are almost exclusively sarcomatous. Stemming from wolfian duct residua, they are of that group of mesenchymal tumors which may arise in the orbit, nasopharynx, and common bile duct; and are identical in most respects with the rhabdomyosarcomas of the prostate in the male child and of the vulvo-vaginal areas in the female child. These tumors are commonly botryoid in configuration and the bulk of the visible intravesical neoplasm usually consists of gray-pink grape-like tumor clusters. Immature or mature striated muscle fibers are the distinctive histologic features.

The symptom complex which sarcomas produce in children are almost always identical and are characterized by the sequence of events in this child's illness. The micturitional symptoms of irritation in the absence of actual infection are due to the encroachment on the bladder lumen by the tumor. The massive size attained by the tumor before diagnosis, as well as the peculiar delay in onset of local or distant metastases, reflects the muscular rather than epithelial site of derivation.

The arteriographic findings in this case were valuable not only as the first documentation of the arterial pattern of a rhabdomyosarcoma of the bladder in a child, but in assuring prompt diagnostic definition of the origin of the tumor, in delineating the lack of contiguous structure infiltration or local metastasis and in demonstrating the origin of the major tumor arterial blood supply. The information allowed cystectomy to be accomplished quickly and bloodlessly. The tumor vascular pattern was thoroughly distrib-

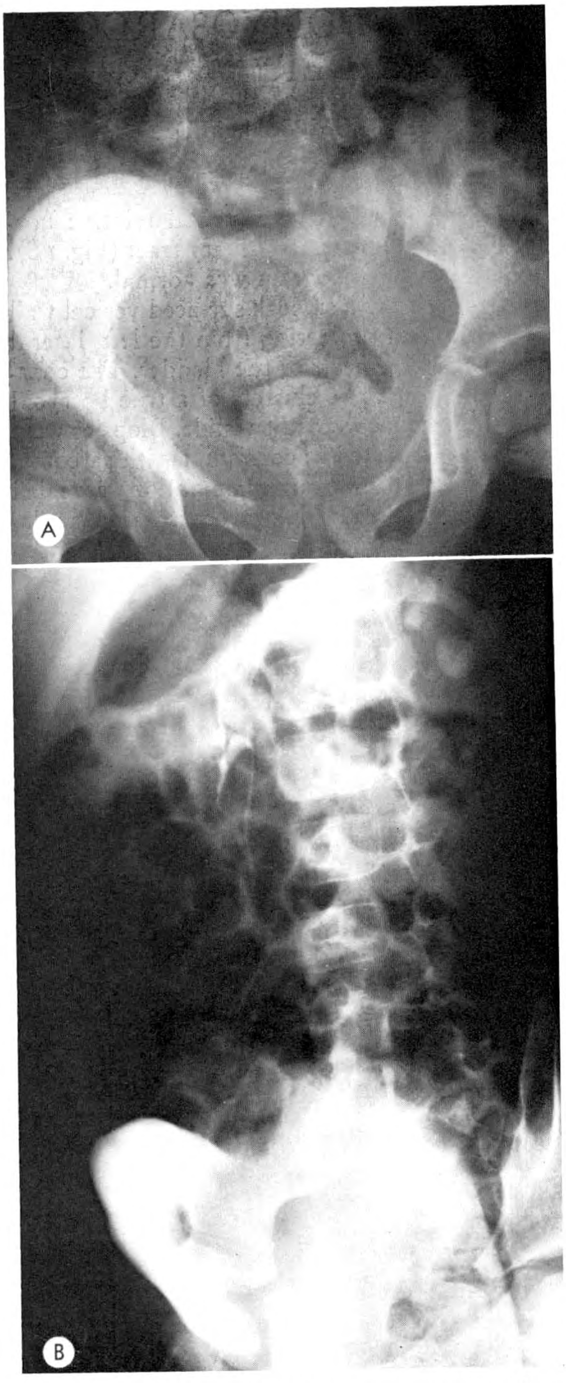

FIG. 1. (*A*) Anteroposterior roentgenogram from cystogram showing marked displacement of bladder superiorly and to the right. The bladder mucosa appears intact. (*B*) Right posterior oblique pyelogram demonstrating anterior displacement of bladder by large left pelvic mass. There is hydronephrosis of left upper urinary tract.

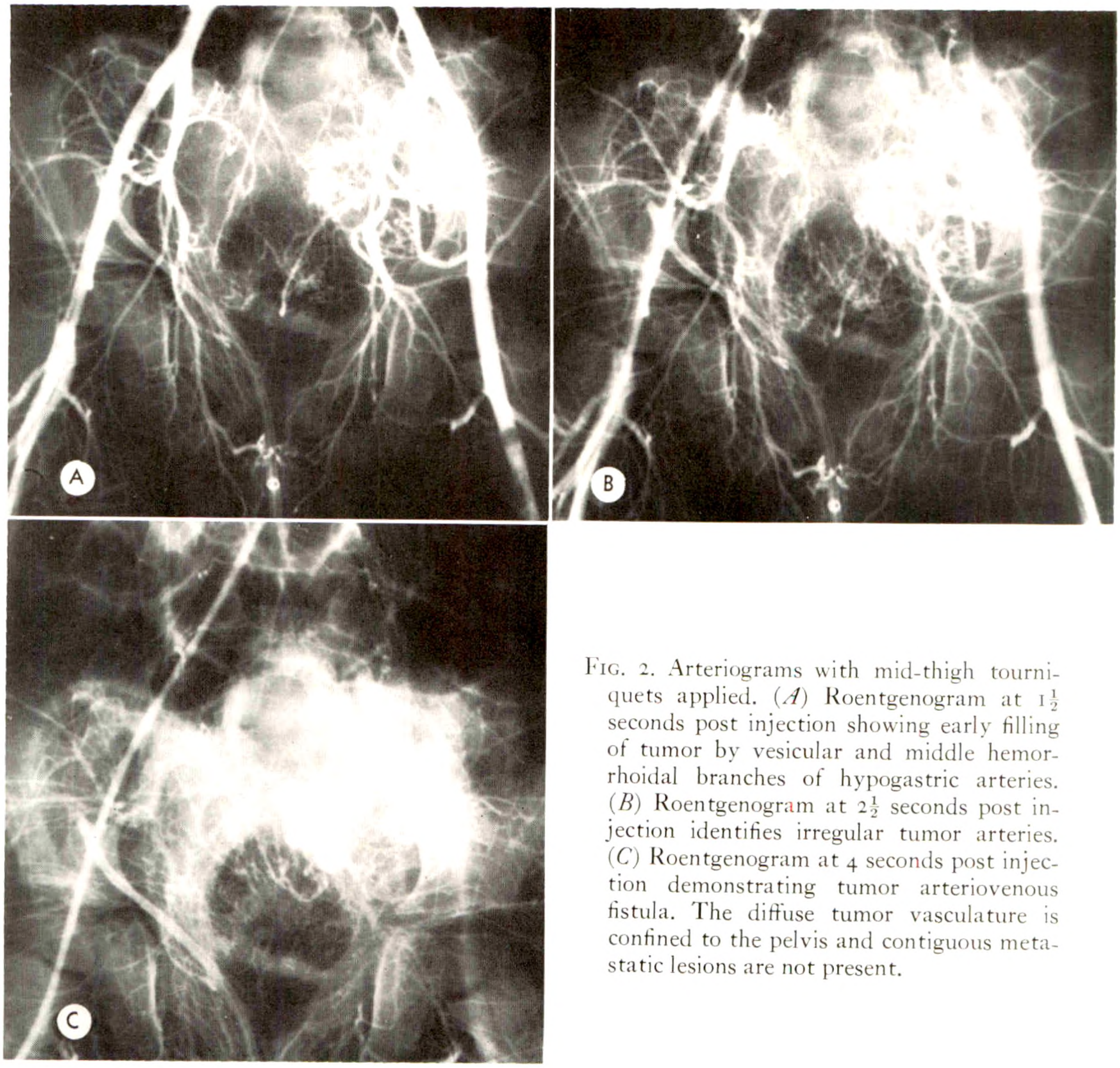

Fig. 2. Arteriograms with mid-thigh tourniquets applied. (*A*) Roentgenogram at $1\frac{1}{2}$ seconds post injection showing early filling of tumor by vesicular and middle hemorrhoidal branches of hypogastric arteries. (*B*) Roentgenogram at $2\frac{1}{2}$ seconds post injection identifies irregular tumor arteries. (*C*) Roentgenogram at 4 seconds post injection demonstrating tumor arteriovenous fistula. The diffuse tumor vasculature is confined to the pelvis and contiguous metastatic lesions are not present.

uted throughout the entire tumor mass. Arteriovenous laking was no more prominent in this case than in the embryonal or Wilms' type of tumor.

Surgery is the treatment of choice. Not infrequently, significant palliation may be achieved with radiation therapy. The possibility of selective arterial infusion with chemotherapeutic agents in appropriate cases of solid embryonal tumors should be more extensively explored.

CONCLUSION

The arteriographic study of rhabdomyosarcoma of the urinary bladder in childhood is presented and the diagnostic and therapeutic potentials of such studies are discussed. A brief résumé of the characteristic clinical and histologic findings is given.

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ANALYSIS IN DEPTH OF BLADDER CANCER TREATED BY SUPERVOLTAGE THERAPY*

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BLADDER cancer affects the elderly population which is exposed to the risks of also dying from other diseases directly unrelated to the cancer. Depending on the age of the patients, the proportion dying from unrelated causes may be considerable. Thus, the presently used survival rate is a poor end point criterion of the assessment of the results of treatment in bladder cancer and the efficacy of different forms of treatments may not be apparent. This may be one of the reasons for the general lack of agreement in the method of treatment for bladder cancer. Although there have been numerous reports on the specific types of treatments for bladder cancer, obtained retrospectively from selected populations, most of the data have been analyzed by descriptive statistical techniques and often the conclusions obtained have been misleading.

In this paper an attempt is made to find out more about bladder cancer than previously reported by the use of newer methods of statistical analysis and to suggest a better method of the reporting of the results of treatment.

CLINICAL MATERIAL AND METHOD OF ANALYSIS

This series consists of 137 cases of cancer of the urinary bladder treated at the Strong Memorial Hospital, Radiation Therapy Center, between April, 1952 to April, 1964. In a previous publication,[10] the results of the first 61 consecutive cases from this group of patients were reported.

The radiation source was either the 1 mev. G.E. resonance transformer roentgen ray or the Picker Co^{60} teletherapy unit. Treatment of patients was distributed equally between the two units, the patients from the earlier period of this study being treated on the roentgen-ray and those from the later period, on the Co^{60} units. The treatment techniques have been modified slightly since the previous report. Patients with Stage B_1 and B_2 lesions received radiation to the entire true pelvis through a 10×12 to 13×13 cm.² field by a three field cross-fire, by rotational or by oscillational techniques, to a cumulative dose of 4,000 r in 4 weeks. Thereafter, the fields were reduced to approximately 8×8 cm.² to include only the bladder and an additional cumulative dose of 2,000 r was delivered in approximately 1.5 weeks. Patients with Stage C and D lesions received 6,000 r to the entire true pelvis in 6 weeks through a 10×15 to 15×15 cm.² field by rotational techniques. The oscillational technique was employed in 4 per cent of the cases, the rotational technique in 82 per cent and the fixed field technique in 14 per cent. The tumor doses varied from 1,000 to 6,500 r and 85 per cent of the cases received more than 5,000 r.

The patients were clinically classified according to Marshall's anatomic stage[6] and according to Rubin's group.[10] The data were analyzed with respect to the following clinical, pathologic or radiotherapeutic variables referable to the time of admission or to the time of onset of therapy: sex, age,

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condition of patient; associated diseases such as hypertension, cardiovascular and chronic pulmonary diseases; symptoms such as hematuria, dysuria, frequency, nocturia, pelvic pain, and weight loss; physical or laboratory findings such as residual urine, prostatic hypertrophy, cystitis, pyelonephritis, ureteral obstruction, blood urea nitrogen over 35 mg. per cent and hematocrit below 35 per cent; previous treatments such as fulguration or transurethral resection, segmental resection, cystectomy and radioisotopic applications; interval between the first urologic treatment and radiotherapy; histologic type; histologic grade; region of bladder involvement; radiation techniques; immediate radiation reaction such as dysuria, frequency and diarrhea, and the time of maximal degree of each of these symptoms after onset of therapy; hemostasis (subsidence of hematuria) and the time of subsidence after onset of therapy; tumor regression and time of complete regression from the final day of therapy; and the follow-up status of the patients.

The follow-up status of each patient was ascertained by careful clinical examinations and by repeated cystoscopic procedures at irregular intervals of 1 to 3 months and also by autopsy when information was available.

Although the specific causes of deaths were often difficult to ascertain, even with autopsy information, patients who had at the time of their deaths generalized metastasis associated with any one or combinations of the following conditions: cachexia, pneumonia, anemia, uremia or cardiorespiratory failure; or no generalized metastasis but had uremia and/or pyelonephritis secondary to bilateral ureteral obstruction due to local recurrence or persistence of cancer were classified as patients dying of cancer or of its effects. Those who died of localized disease without bilateral ureteral obstruction and showed no clinical evidence of generalized cancer but had other diseases which caused their demise were classified as dying of other causes with the presence of cancer; and those who had no clinical evidence of recurrence or metastasis of cancer during their course of life were classified as dying of other causes without the presence of cancer. The latter group of patients were in a practical sense "cured" of cancer.

Various statistical procedures were used in the analysis of the patients' data, *e.g.*, the Student t test, the chi-square test of independence, analysis of variance, the Berkson-Gage method of calculation of survival rates[8] and the discriminant analysis for several groups.[3] Before using some of these procedures, histograms of each of the variables, considered for analysis, were plotted and the necessary transformations of the values were carried out in order to obtain the required distributions. For example, the linear survival time values were transformed into logarithmic values in order to produce approximately a normal frequency distribution for their utilization in the discriminant analysis. Calculations of the survival rates and the discriminant analysis were carried out by means of the University of Rochester, IBM 7074 electronic digital computer.

RESULTS

A. ANALYSIS OF PATIENTS ACCORDING TO RUBIN'S GROUP AND MARSHALL'S STAGE

I. *Clinical and Physical Findings.*

There were 22 patients in Group I, 81 in Group II, 34 in Group III (Stage D), 41 in Stage OAB$_2$ and 62 in Stage B$_3$C. The analysis of each of the variables was carried out according to these respective groups or stages; however, due to the extensiveness of the data, the tables have not been included in this report.

1. *Sex:* In the entire series there were 79 per cent male and 21 per cent female patients having similar distributions in all groups or stages.

2. *Age:* At the time of onset of supervoltage therapy the per cent frequency distribution of patients in the fourth to the ninth decades were 1, 3, 15, 27, 38 and 16, respectively. There were no significant differences in distribution among the groups

or stages. The average age was 70.5 years. No difference was found between the average ages of both sexes.

3. *General Status:* A clinical diagnosis of arteriosclerotic heart disease, hypertension, heart failure or chronic pulmonary disease was made in 45 per cent of the patients. Their per cent frequencies were significantly higher in Group II and Stage B_2C, 50 and 60 per cent as compared to 30 to 35 per cent for the others.

4. *Symptoms:* At the time of admission approximately 75 per cent of the patients had hematuria, 54 per cent had dysuria, and 65 per cent had nocturia or frequency. No differences in distributions were found among the groups or stages. Weight loss was present in 15 per cent and pelvic pain in 23 per cent of the patients. The per cent frequencies of these symptoms were significantly higher in Group III (Stage D), 30 and 50 per cent as compared to less than 15 per cent in the others, respectively.

5. *Physical and Laboratory Findings:* Residual urine was found in 18 per cent, prostatism in 38 per cent, cystitis in 33 per cent, pyelonephritis in 4 per cent, radiologic evidence of ureteral obstruction in 36 per cent, increased blood urea nitrogen in 4 per cent and anemia in 9 per cent of the cases. The per cent frequencies of the latter three findings were significantly higher in Group III (Stage D) than in the other groups or stages, 65, 12 and 23 per cent as compared to less than 34, 2 and 4 per cent, respectively.

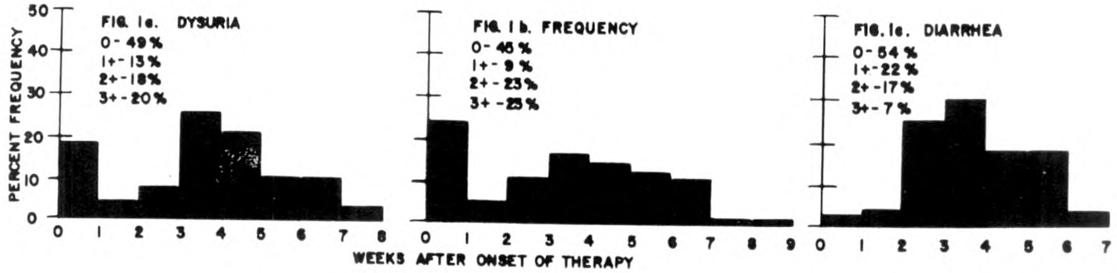
6. *Previous Treatments:* Seventy-five per cent of the patients were treated by transurethral resection or fulguration procedures (55 per cent) or by segmental resection (20 per cent). Only 6 per cent had an intracavitary radioisotopic procedure and 1 patient in the group (Stage D) had total cystectomy. There were no differences in the distribution of the various modalities of treatments among the groups or stages. Regardless of the group or stage, the average interval between the first urologic treatment and supervoltage therapy was approximately 15 months.

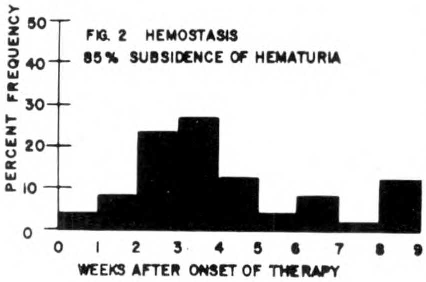
II. *Pathologic Findings.*

1. *Histology and Grade:* Ninety-three per cent of the cases were diagnosed as transitional cell carcinoma, 5 per cent as epidermoid carcinoma, 1 per cent as sarcoma and 1 per cent as adenocarcinoma. There were 9 per cent of Grade I, 17 per cent of Grade II, 38 per cent of Grade III, 31 per cent of Grade IV and 5 per cent of Grade V lesions. Most of the Grade IV lesions were found in Group III (Stage D). It must be mentioned that Group I, by definition, does not contain lesions higher than Grade II; therefore, the bias is self-imposed; however, the proportions of high grade lesions were greater in Stages B_2C and D than in Stage OAB_1.

III. *Supervoltage Therapy.*

1. *Immediate Radiation Reaction:* Figure 1, *a*, *b* and *c* shows the per cent frequency distributions of the maximal degrees of urinary frequency, dysuria and diarrhea after the onset of therapy. These values are not the same as those obtained on admission for the following reasons: the time elapse between admission and onset of therapy; the interposition of urologic and other procedures; the differences in the evaluation of symptoms among different physicians; etc. The degree of frequency or diarrhea was graded according to the number of daily bladder or bowel movements, *e.g.*, Grade 1 for 2–4 times, Grade 2 for 5–8 times and Grade 3 for more than 8 times daily. The degree of dysuria was graded subjectively from 0–3. It is seen that nearly half of the patients did not have any of these symptoms at or after the onset of therapy. Of those who had frequency or dysuria, the per cent frequency of symptoms decreased after 1 week, increased to maximum between 3 to 5 weeks and decreased to low values at 8 or 9 weeks. In some of the patients the initial maximal symptoms may have been due to the cancer or to the cystoscopic procedure. On the contrary, the per cent frequency of maximal diarrhea increased from initially low values





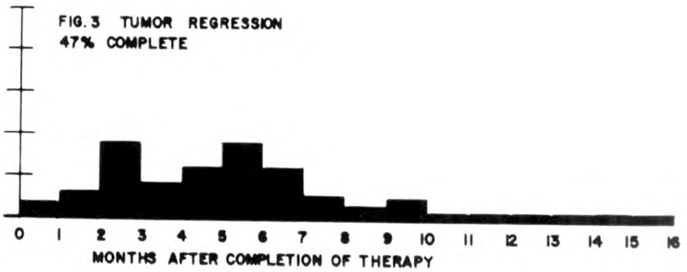


Fig. 1. (*a*, *b* and *c*) Immediate reactions during supervoltage therapy of bladder cancer.

Fig. 2. Subsidence of hematuria due to bladder cancer with supervoltage therapy.

Fig. 3. Complete tumor regression with supervoltage therapy of bladder cancer.

to maximum between 2 to 4 weeks and decreased to low values at 6 to 7 weeks. These per cent frequency values of the maximal complaints should not be confused with those without regard to maximal complaints. The former specifically indicates that, under these conditions of therapy, the maximal degree of symptoms occurs at the specified time intervals and tells nothing of their persistence thereafter, whereas the latter indicates the reverse. There were no differences in the per cent frequency distributions of symptoms with respect to time after the onset of therapy among the groups or stages. Since various types of medications were administered to combat these symptoms, these per cent frequency distribution values of radiation-induced symptoms are likely to be different from those of patients not given these medications.

2. *Hemostasis:* At the onset of therapy the per cent frequency of hematuria was 65 as compared to 75 on admission. This slight decrease in incidence may be partly due to the partial removal of cancer at the time of cystoscopic examination before treatments. Hemostasis was achieved in 85 per cent of the patients. Figure 2 shows that by 5 weeks of therapy or at a cumulative tumor dose of approximately 5,000 r, 75 per cent of the patients had complete subsidence of hematuria, 60 per cent had subsidence between 2 to 5 weeks, and 12 per cent between 2 to 3 months. There were no differences in the chronologic patterns of the per cent frequency distribution among the groups or stages.

3. *Tumor Regression:* Seventy per cent of the patients had a sufficiently adequate number of repeated cystoscopic procedures to make it possible to assess their maximal tumor response. Of these, 47 per cent had complete regression, 22 per cent had partial and 31 per cent had no regression. Figure 3 shows that approximately 80 per cent of the complete regressions occurred by 7 months after the completion of therapy, 68 per cent between 2 to 7 months, and 10 per cent after 10 to 12 months. The reasons for the broad distribution in the per cent frequency values may be partly due to the irregular intervals of cystoscopic examinations; however, it is not uncommon to encounter situ-

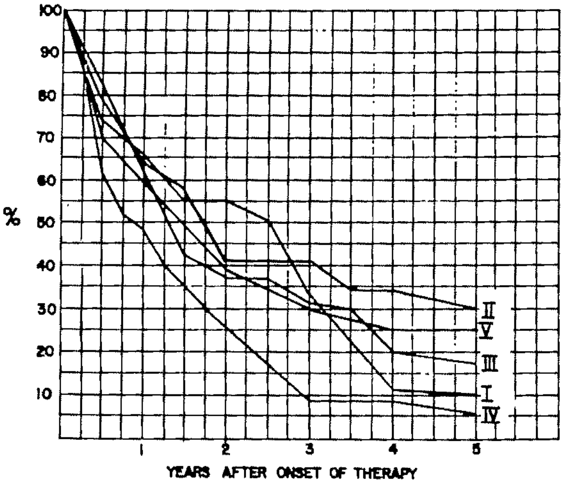


Fig. 4. Survival rate according to histologic grade of bladder cancer after supervoltage therapy.

ations in which bladder cancer may persist for many months, and then suddenly not be evident at subsequent examination. The per cent frequency of complete regression was significantly less in Group III (Stage D) than in the other groups or stages, 19 per cent as compared to 55 to 60 per cent. The distribution with respect to time after therapy did not differ among the groups or stages.

4. *Survival after Supervoltage Therapy:*

(a) Histologic Grade. Figure 4 shows the survival curves of the patients with respect to histologic grade. Although the histologic grade of bladder cancer has been reported to be of prognostic importance,[4,12] in this series as well as in that of Miller *et al.*,[7] there were no significant differences in the survival curves with respect to grade. One of the reasons for this finding may be due to the fact that the biopsy specimens obtained from externally irradiated patients are not representative samples of the entire tumor.

(b) Clinical Stage and Group. Figures 5 and 6 show the survival curves (solid lines) of the patients with respect to groups and stages. The difference between the survival curves of Groups I and II was not significant, but the differences between each of these curves and that of Group III (Stage D) were significant. On the other hand, the differences among the survival curves of Stages OAB$_1$, B$_2$C and D were significant. The reason that the curves of Groups I and II are not different is that since Group I, by definition, contains Stages OAB$_1$ but no histologic grade higher than II, the removal of the higher but early stage lesions from Stage OAB$_2$ lesions and their placement into a group with Stages B$_2$C lesions, decreases the survival rate of the former and increases that of the latter group. Hence, when the grade of cancer is used for classification purposes, it is important that it represent the major portion of the tumor in a patient.

(c) Recurrence-Free Rate versus Survival Rate. Figures 5 and 6 also show that the recurrence-free rates (dotted lines) of the respective groups or stages are lower than the survival rates, especially in patients with Group I and Stage OAB$_1$ lesions. In these patients the cancer continues to recur even at 5 years after therapy, whereas in patients with Group II and Stage B$_2$C lesions the

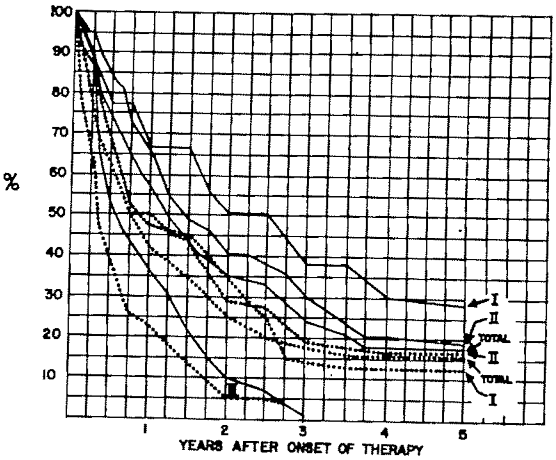


Fig. 5. Survival (solid lines) and recurrence-free (dotted lines) rates according to Rubin's group of bladder cancer after supervoltage therapy.

recurrence-free and the survival rates are approximately the same at 3 to 4 years. In Group III (Stage D) the recurrences continue until all the patients are dead by 3 years. In the entire series 23 per cent of the recurrences were treated by fulguration or transurethral resection, 5 per cent by simple or total cystectomy, 15 per cent by irradiation and 6 per cent by chemotherapy. It is evident that survival rates, themselves, are not the optimal end point of measurement of the efficacy of supervoltage therapy in bladder cancer.

(d) Region of Bladder Involvement. Figure 7 shows the survival curves of patients with Stages O to C lesions divided into groups with lateral wall, trigone plus posterior wall or bladder neck involvements. The difference in the curve of the group with lateral wall involvement and that with bladder neck involvement was significant, but the differences in the curves among the other groups were not.

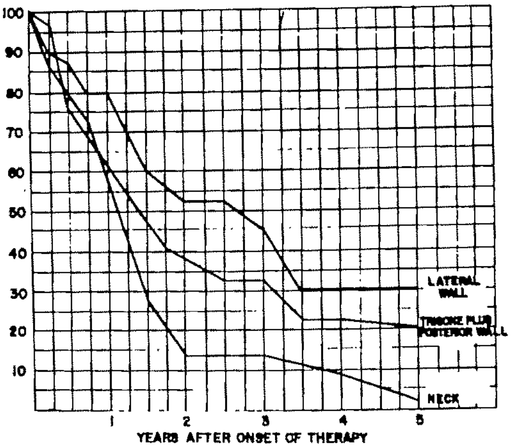


Fig. 7. Survival rate according to region of bladder involvement in bladder cancer after supervoltage therapy.

(e) Radiation Dosage. Figure 8 shows the survival curves of each of the three groups with respect to cumulative tumor doses of less than 5,000 r (dotted lines) and of doses more than 5,000 r (solid lines). Because of the few cases in each of the former dose groups, the differences between the curves with respect to cumulative tumor doses were not significant for each of the three groups. However, the combined curves of these groups were significantly different with respect to the two dose ranges. The major reasons that some of the patients received less than 5,000 r were as follows: the reduced tolerance to treatments due to advanced cancer;

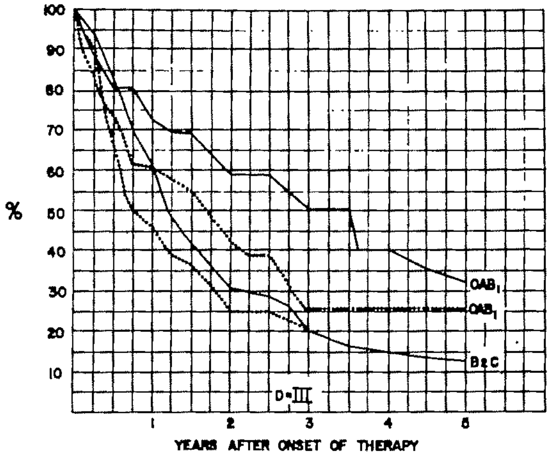


Fig. 6. Survival (solid lines) and recurrence-free (dotted lines) rates according to Marshall's stage of bladder cancer after supervoltage therapy.

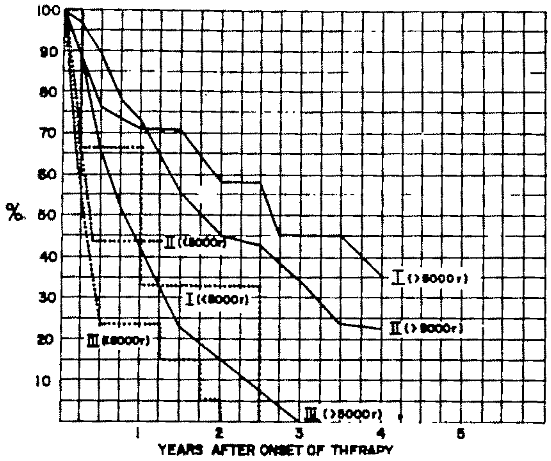


Fig. 8. Survival rate according to radiation dosage and Rubin's group of bladder cancer after supervoltage therapy. Tumor dose of more than 5,000 r is indicated by solid lines and less than 5,000 r by dotted lines.

palliation was the aim of therapy; and the failure or refusal of the patient to complete the prescribed course of treatment.

5. *Causes of Death:* In the entire series 12.4 per cent were alive with cancer, 11.8 per cent were alive without cancer, 3.7 per cent were alive but the cancer status was not ascertained, 48.5 per cent were dead due to cancer, 13.8 per cent were dead due to other causes with cancer present, 8.0 per cent were dead due to other causes without cancer present, 1 patient was dead but his cancer status was not ascertained, and 1 patient was lost to follow-up.

Of the 71 per cent of the patients who were dead and whose cancer status was known, 57 per cent in Group I had died of cancer, 65 per cent in Group II, 90 per cent in Group III (Stage D), 55 per cent in Stage OAB$_1$ and 67 per cent in Stage B$_2$C. The per cent frequency of deaths due to cancer was significantly higher in Group III (Stage D) than in the other groups or stages.

6. *Complications of Therapy:* There have been no strict criteria in the definitions of radiation complications. For example, in radiation cystitis, various degrees of symptomatic cystitis may be present. Some patients may complain of mild but persistent symptoms lasting until their deaths whereas others may complain of severe but temporary symptoms. Quite often it is difficult to distinguish whether the symptoms are due to the persistence of cancer, to the radiation treatments or to both. A good proportion of the patients with cystitis have infected urine and it is impossible to determine whether their symptoms are due to infection or to radiation, and whether the patients would not have had bacterial cystitis if it was not for the necessity of repeated cystoscopic examinations. Having defined radiation cystitis as cystitis symptoms lasting more than 6 months without evidence of infection by culture or of cancer by biopsy, there were 4 cases that met this criterion. There were 5 other patients with prolonged duration of symptoms but with positive urine cultures for bacteria. A contracted bladder with a capacity less than 40 cc. was present in 3 cases and these were also included with the patients with persistent cystitis. Ulceration and bleeding requiring blood transfusions occurred in 3 cases. One of them had a total cystectomy procedure and tumor was found in the bladder specimen. Bowel necrosis occurred in 1 patient. Under these specifications the complication rate was 6 per cent (8/137) and, including the 5 patients with positive urine cultures, the rate was 10 per cent (13/137). There were no deaths which could be ascribed to the supervoltage therapy procedure.

B. ANALYSIS OF PATIENTS ACCORDING TO THE CAUSES OF DEATHS

At the time of the undertaking of this study, 71 per cent (97/137) of the patients had died of various causes. Of these 69 per cent had died of cancer (Class X), 20 per cent of other causes with the presence of cancer (Class Y) and 11 per cent of other causes without the presence of cancer (Class Z). Seven variables, namely, age, stage of cancer, grade of cancer, duration of treatment, cumulative tumor dose, survival and recurrence-free times, were chosen arbitrarily for analysis by the discriminant procedure. Class Z, "cured" patients, was discriminated from the other classes because of its long average survival time of 42.5 months, as compared to 10.3 and 10.9 months for Classes X and Y, respectively. In statistical terms, the generalized, multivariate null hypothesis that the three classes have similar orientation in space is not tenable ($p < 0.001$).

The average recurrence-free times of the latter two classes were 4.5 and 3.6 months, respectively. Survival and recurrence-free times contributed to 85.2 per cent of the discriminating power, stage to 14.7 per cent, age to 0.11 per cent and others to none. It is interesting to note that the recurrences occurred approximately 6 months before the deaths of the patients in Classes X and Y.

Since the survival and recurrence-free times are inherent features in the selection of patients in Class Z, as these were shown to be the discriminating variables, the analysis was carried out by excluding these two variables. The results showed that Class Y was discriminated from the other two classes, and stage contributed to 99 per cent of the discriminating power. It is mentioned, here, that only 4 of the 19 patients in Class Y required definitive retreatments, *i.e.*, 3 required fulguration and 1, re-irradiation.

Analysis of variance and multiple t test on single variables showed that the average survival and recurrence-free times were significantly higher in Class Z than in the other two classes, the average stage was significantly lower in Class Y (2.8 as compared to 4.0 and 3.5 for Classes X and Z), and average age was significantly lower in Class X (68.7 as compared to 74.8 and 73.5 in Classes Y and Z). The average histologic grades, cumulative tumor doses and durations of treatment were similar in all three classes.

Chi-square tests were performed on the distribution of each of the variables, mentioned in the previous sections, among the classes. The only difference that was found to be of significance was the higher incidence of trigone plus posterior wall and bladder neck involvements in Class X than in the others.

DISCUSSION

The purpose of using statistics for the analysis of single variables (univariate analysis) of patients in this study is to standardize the differences in the distributions or in the mean values of the variables at the maximally accepted level of significance of say 5 per cent. For example, in the chi-square test of homogeneity of distribution of variable between two groups of a sample size of 10 subjects each, the difference must be approximately 50 per cent in order for it to be of significance at this level, in two groups of 20 subjects each, the difference must be approximately 35 per cent, in two groups of 40 subjects each, approximately 25 per cent, etc. However, since statistical assumptions are often not met in retrospective data, the results of statistical analysis of such data must be interpreted with caution.

Far too often in the medical literature differences in values, which can occur by chance alone under the above stated statistical conditions, are stated to be of significance or of no significance depending on certain medical preconceptions. By using statistical criteria the differences in values, which may appear large or small especially when converted to percentage values, can be accepted as being significant or not at a prescribed level, depending on the sample size and/or dispersion.

The discriminant analysis for several groups is used since it is known that most medical data are multivariate in scope. In the analysis of the data from this series, all of the variables used were not handled by this procedure because of the small sample size and the differences in population distribution of some of the variables. Hence, only seven variables were analyzed with the intent of finding out which of these would contribute most in discriminating the three classes of patients.

The population of bladder cancer patients reported herein is older than that reported by some of the authors. For example, the average age in this series is 70.5 years, as compared to 56 in the series of Schwartz *et al.*,[11] 58 in Whitemore and Marshall's[15] group, 61.3 in Claridge and MacDougall's[2] cases, 62.6 in Thompson's[13] group, and 66.5 in Watson and Campbell's[14] cases. Furthermore, 54 per cent of the patients are over 70 years, as compared to 23 per cent in the cases of Miller *et al.*[7] and 14 per cent in the series of Dean *et al.*[4] Therefore, it is not surprising to have found a high incidence of cardiovascular and chronic pulmonary diseases. Also 75 per cent had been treated previously with an average delay of 20 months. In other words these patients were of poor risk for radical therapy because of their advanced age, associated diseases and advanced cancer. Despite these disadvantages, it was possible to arrest the cancer in 31 per cent of the group of dead patients so that they could die of other causes, not directly related to the cancer, and to attain an "absolute cure" of 11 per cent with a low incidence of complications.

The aforementioned are only a few of the many examples of differences in distribution of variables from one selected population of bladder cancer patients to another. Because of this realization, no comparison of survival rates of this series has been made with those of others.

The analysis of each of the variables among the groups or stages shows that the stage of bladder cancer, directly paralleled by the increased incidence of adverse clinical or laboratory findings, *e.g.*, weight loss, pelvic pain, ureteral obstruction, increased blood urea nitrogen, anemia, and nonresponsiveness of cancer to irradiation, is the most important in predicting the survival of the patients. Independent of stage, the involvement of bladder neck region reduces their survival. However, the result of discriminant analysis fails to show that the earliness of stage is of major significance in the "cure" of cancer patients. It implies that the patients who died of other causes with cancer present had an earlier initial stage, but because of their advanced age and the presence of other age-dependent diseases, they died of these diseases rather than of their bladder cancer. Because the time of recurrences was the same in patients who died of cancer and in those who died of other causes with cancer present, it is speculated that the cancer was less malignant in the latter group, although many other variables, some of which may be important in the predictability of "cure" of cancer, have not been considered.

Survival rate alone, is not a suitable criterion of the end point of success in the treatment of bladder cancer. From published reports[1,14] it can be estimated that in the elderly age group approximately 20 to 30 per cent of the patients with bladder cancer die of seemingly unrelated causes. With such high proportions of patients dying of these causes rather than cancer, the efficacy of a treatment procedure may not be apparent, since in the present status of cancer therapy only small percentages in improvements are expected. Furthermore, since reports show that the crude survival rates decrease with increase in age,[5,18] it is assumed that this decrease was due to an increase in the incidence of deaths due to unrelated causes.

Our figures show that nearly all of the recurrences, local, regional, or distant, occurred within 3 years after therapy. Miller *et al.*[7] estimate that 95 per cent of local recurrences in their series occurred before 3 years, although they state that the recurrences may be often difficult to distinguish from new primary lesions.

In conclusion, it is stated that the results of supervoltage therapy of bladder cancer in this series, consisting of elderly patients, is encouraging, *i.e.*, 31 per cent of them did not die of their cancer. The analysis of clinical data in terms of recurrence-free and survival rates, as well as of the causes of death, is a better method of assessment of results in the treatment of bladder cancer than in terms of survival rates alone, since a considerable portion of the patients may die of other causes with or without recurrences. However, due to the many differences in variables from one selected population to another, the comparison of results among series is difficult. Comparison of results among sample populations given various types of treatments is possible only by clinical trials based on sound statistical principles. Although the commonly defined variables, *e.g.*, age, stage and grade, have been purported to be of significance in the survival of bladder cancer patients, they may not be as important predictor variables in the curability, as supposed.

SUMMARY

1. The results of a detailed analysis of 137 cases of elderly patients with bladder cancer, treated by supervoltage therapy, are presented.

2. The 5 year actuarial survival rates were 17 per cent for the entire series, 28 per cent for Group I, 19 per cent for Group II, 0 per cent for Group III (Stage D), 33 per cent for Stage OAB_1 and 13 per cent for Stage B_2C. Nearly all recurrences occurred before 3 years after therapy.

3. Thirty-one per cent of the patients died of other causes with or without the recurrence of cancer. In the class of patients who died of other causes with recurrence, only 4 of the 19 patients required definitive treatments for their recurrences.

4. The analysis of clinical data in terms of recurrence-free and survival rates, as well as of the causes of death, is a better method of assessment of results in the treatment of bladder cancer than in terms of survival rates alone.

5. The importance of the undertaking of clinical trials for the comparison of results of two or more methods of treatment is emphasized.

6. The further analysis of retrospective data from large populations of bladder cancer patients by modern statistical methods may yield further information about the classification and prognosis of bladder cancer than possible by routine statistical methods.

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CYSTOURETHROGRAPHY: AN EVALUATION OF METHOD*

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CYSTOURETHROGRAPHY has undergone radical change in the past 5 years. Prior to 1958 a cystogram commonly consisted of a single roentgenogram after the bladder was filled in a blind manner with an arbitrary amount of opaque material. The procedure was frequently performed on the cystoscopic table following cystoscopy in an anesthetized patient. Visualization of the bladder occurred only during the fraction of a second it took to expose the film. Voiding urethrograms were made in much the same manner as the opaque material ran passively through the urethra.

The beginning of widespread use of cineroentgenography in the examination of the urinary tract in 1958 stems from the early work of Narath.[11] Cineroentgenographic techniques were later described and advocated by Benjamin *et al.*,[2] Hinman *et al.*,[6] and by Garrett and Klatte[5] and quickly revealed the inadequacies of the previous methods. Cineroentgenography became the magic word in cystourethrography and the esteem in which it is held is best stated by Rhamy *et al.*,[12] "This examination has been most helpful in demonstrating fleeting vesicoureteral regurgitation and delineation of the bladder neck. The proper diagnosis in many of these cases would have been missed by conventional examination, and in many more an incorrect diagnosis of vesical neck obstruction would have been made."

The chief contribution of cinecystourethrography, however, was that it revealed the importance of performing the examination with fluoroscopy which is a necessary part of the cine process. Some observers were dissatisfied with the cine films because of poor detail inherent in the cine filming process. Davis *et al.*,[4] in 1961, described a method in which cystourethrography was performed with fluoroscopy, as in the cine method, but using multiple, phototimed, spot films instead of cine films. This method has gained acceptance as additional reports attested to its merits.[3,8,9]

There have, therefore, been established two schools of thought concerning the proper method of performing cystourethrography, the cine and the spot film methods. The purpose of this paper is to report the results of a study evaluating the two.

MATERIAL

Ninety patients (45 females and 45 males) were examined by both cine and spot film cystourethrography. The procedures were performed in the radiology department in nonanesthetized, nonsedated patients. When necessary, immobilization of the patient was by means of a "bratboard" (Fig. 1). Sterile catheterization was performed using either a catheter or a plastic tube ranging in size from 5F to 10F. Fifteen per cent sodium iodide or 20 per cent diatrizoate sodium was used as the opaque medium, it being the same in any

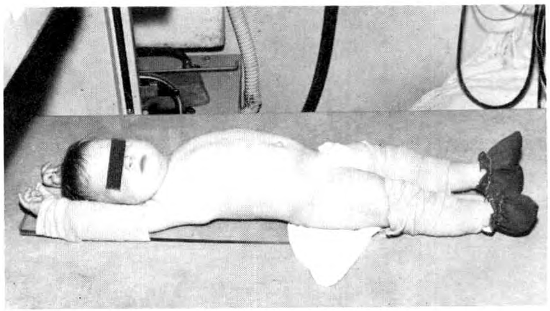

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Fig. 1. Arms and legs are effectively bound to board with ace bandages. Patient is easily moved to any desired position.

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one patient and therefore not a factor in evaluation of the two methods.

All examinations were performed under fluoroscopy. The bladder was filled by hand injection from a 50 cc. syringe, utilizing appearance of bladder, discomfort of patient, presence of reflux and spontaneous voiding around the catheter as criteria of adequate filling. To ensure constant volume and pressure for the two methods, no additional material was injected after adequate filling was determined. Sixteen millimeter cine and 8 inch×10 inch phototimed spot films of the bladder, ureters and upper collecting system were exposed in the anteroposterior, lateral, and both oblique projections. The catheter was then removed, and as the patient urinated, roentgenograms were made of the urethra in the right posterior oblique position by both the cine and the spot film methods (Fig. 2, *A–D*; and 3, *A–D*). Little difficulty is encountered in getting the patient to void if adequate filling of the bladder has been obtained. Even pediatric patients do not urinate on command, and some patience, psychology and experience are required to obtain consistently adequate urethrograms.

RESULTS

The objective of cystourethrography is twofold: (a) to demonstrate pathologic physiology, namely reflux; and (b) to demonstrate pathologic anatomy. The studies were therefore analyzed regarding their capability to detect reflux and to show anatomic detail.

Reflux. Sixty-two (68 per cent) of the 90 patients showed reflux. In all instances the reflux was detected by both methods. It soon became apparent that reflux was almost always identified at fluoroscopy and roentgenograms were made to document it. There were only 3 patients with reflux that was not seen at fluoroscopy, and in each the reflux was demonstrated by both the cine and spot film methods of roentgenography.

In 10 patients cine revealed a transient squirt of reflux. All but one were seen by fluoroscopy and all were shown by the spot films (Fig. 4, *A–D*). During the voiding urethrogram phase of the examination, it is important that the ureterovesical junction be included in both the spot and cine films as fleeting reflux is most likely to occur at this time. Cine has been especially touted as excelling in detecting fleeting reflux, but in this study it was no better than the spot films.

Pathologic Anatomy. A discussion of the photographic and physical principles involved in cine and spot filming is not within the scope of this paper. There are inherent limitations in the cine filming process which prevent it from having the detail and definition possible with spot films. Since cystourethrography is a clinical procedure, it seemed logical to judge and compare the cine and spot film methods on clinical grounds rather than on physical and photographic criteria.

Therefore, the two methods were compared as to their capability to detect certain pathologic features as listed in Table I. The spot film method excelled in demonstrating all abnormalities judged. Cine is particularly deficient in those lesions requiring fine detail such as mild bladder trabeculation and cellule formation, verumontanum hypertrophy and urethral granulomatous defects[1] (Fig. 5). Cine did not possess the fine contrast necessary to identify the double density caused by a ureterocele protruding into the base of the opaque bladder, or the resolving detail to define accurately distal urethral stenosis[10] (Fig. 6). Its diagnostic accuracy increased with the larger diverticula but it still did not provide as high an accuracy as did the spot films.

DISCUSSION

Over 500 additional patients have been examined with spot film cystourethrography alone. During the same period of time only 33 solitary cinecystourethrographies were performed.

Cystourethrography has developed along the principles of most special roentgeno-

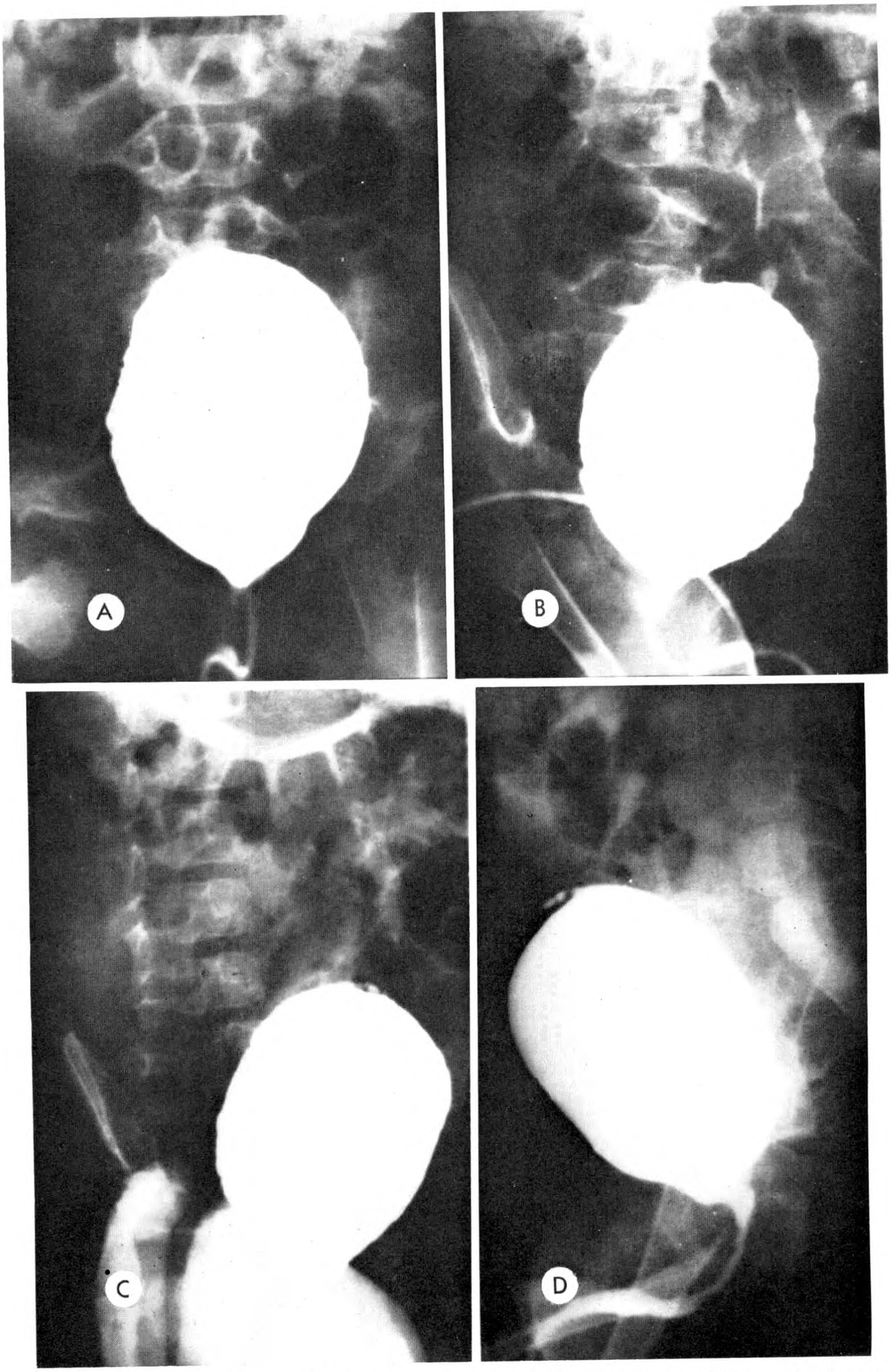

FIG. 2. Spot roentgenograms of the bladder, covering the area of the ureters and kidneys, in the (*A*) anteroposterior, (*B*) lateral and (*C* and *D*) both oblique positions. Note the bladder trabeculation. A small urachal duct remnant is shown in the lower two spot roentgenograms.

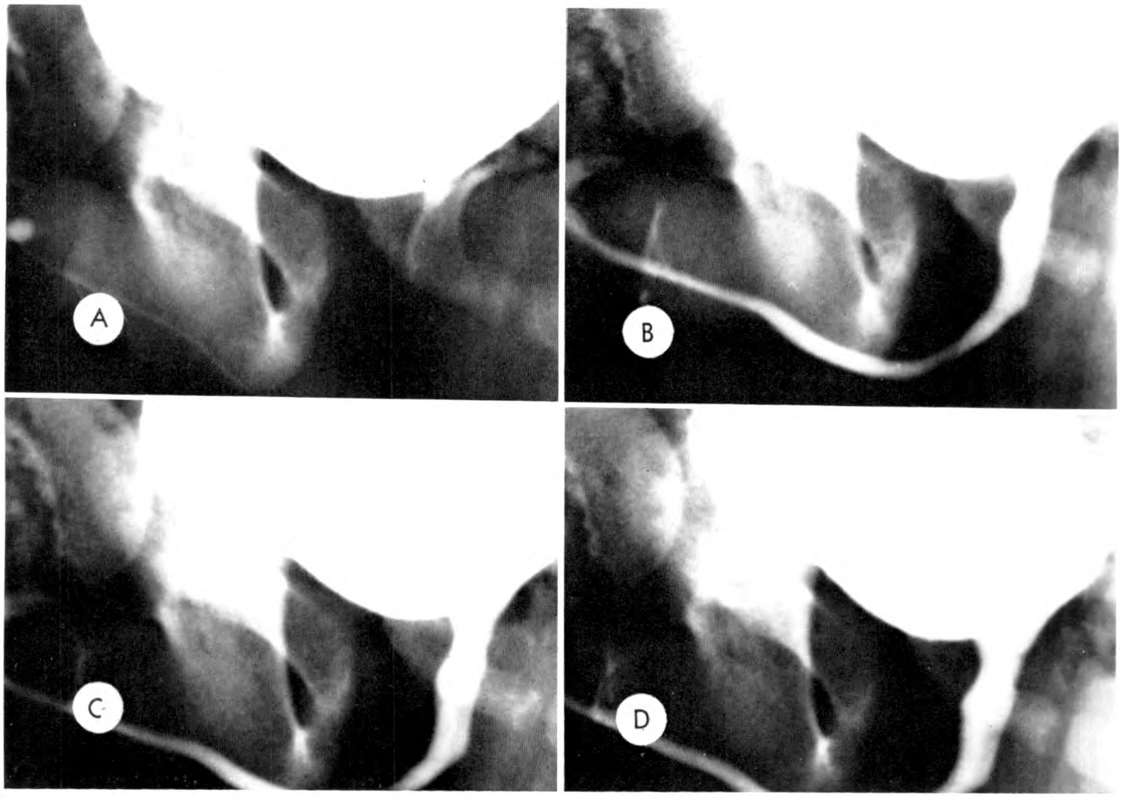

Fig. 3. (*A–D*) Four spot roentgenograms of the urethra taken rapidly during voiding. These were phototimed and all 4 are on one 8 inch×10 inch film. The urethra and base of bladder are shown in the right posterior oblique position.

Table I

COMPARISON OF CINE AND SPOT FILM CYSTOURETHROGRAPHY IN DEMONSTRATING PATHOLOGIC ANATOMY

Abnormality		Cine						Spot Films					
		Positive		Negative		Questionable		Positive		Negative		Questionable	
		No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Bladder	trabeculation cellules	40	44	42	47	8	9	68	75	16	18	6	7
	diverticula	3	3	87	97	0		5	6	85	94	0	0
Hutch Diverticulum		12	13	74	82	4	5	18	20	72	80	0	0
Ureteroceles		0	0	90	100	0	0	3	3	87	97	0	0
Hypertrophy Verumontanum		2	4	35	77	8	19	12	27	31	68	2	5
Utriculus Masculinus		0	0	45	100	0	0	3	7	42	93	0	0
Granulomatous Defects		0	0	45	100	0	0	8	17	36	80	1	3
Distal Urethral Stenosis		2	5	39	86	4	98	7	15	38	85	0	0

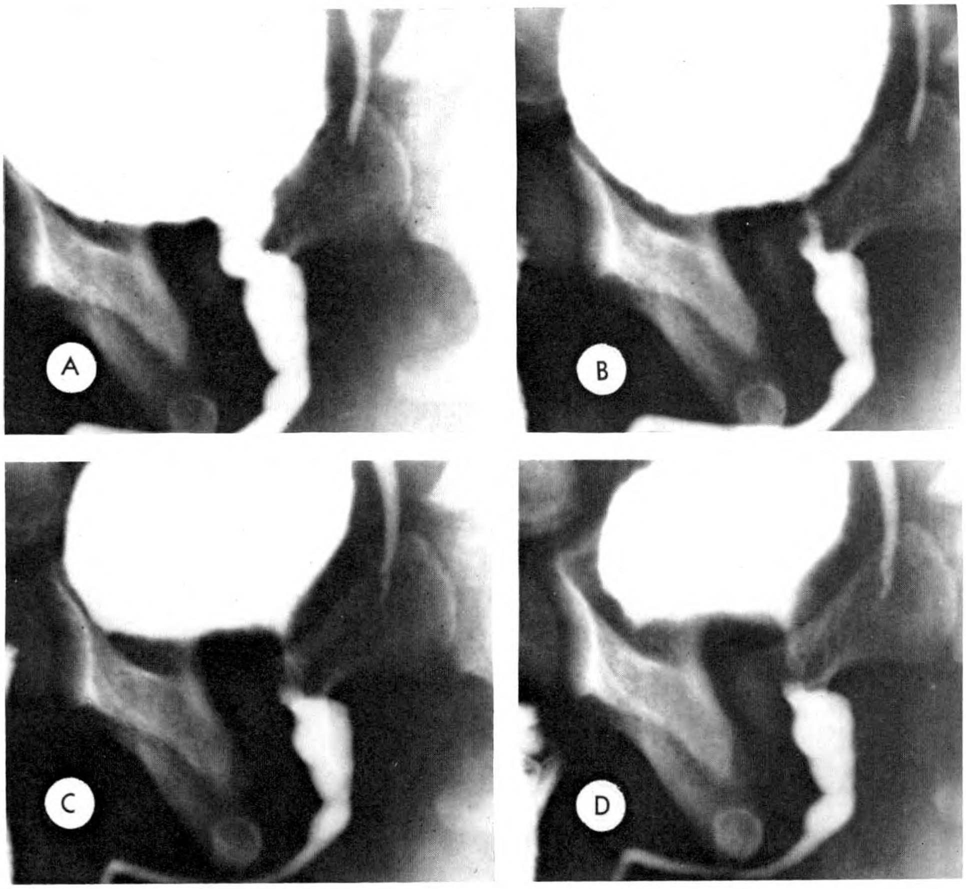

Fig. 4. (*A–D*) Spot roentgenograms of urethra and base of bladder during voiding. Squirt of reflux up left ureter was seen at fluoroscopy and also in the cine films.

logic procedures; *i.e.*, they are performed under fluoroscopy for proper control and observation of pathologic physiology and anatomy. Roentgenograms are made during the progress of the procedure to document abnormal physiology and demonstrate abnormal anatomy, seen or not seen at fluoroscopy. Spot films excel cine in fulfilling these principles for two reasons: (1) a spot film is exposed instantaneously, and fluoroscopically observed abnormal physiology can be recorded on a still film without benefit of motion as afforded by cine. Spasm, atonicity, regurgitation, rigidity and deformity are recorded much the same as they are in an upper gastrointestinal study which has been performed for many years by fluoroscopy with spot filming for documentation and recording; (2) the detail and definition of spot films far exceed those of fluoroscopy because of certain physical and photographic principles. Spot films many times reveal pathology not possibly detectable by fluoroscopy. Cine, on the other hand, because of the principles involved, can show no improvement of the fluoroscopic detail and definition.

Cine filming in cystourethrography is assuming the approximate place it has in other roentgenologic procedures;[13] *i.e.*, to record motion for teaching and research purposes where fine detail of pathologic anatomy is not required.

In our opinion, fluoroscopy has been the most important contribution to cystourethrography. The bladder can be filled consistently in a standardized fashion utilizing its size and contour, appearance of reflux, discomfort of the patient and spontaneous voiding around the catheter as criteria to determine adequate filling. This method of controlled filling has been found to be more reliable than filling with controlled gravity pressure with or without concomitant intravesical pressure readings. Pressure readings as high as 50 cm. water have been shown by fluoroscopy to be greatly variable and unreliable, resulting in inadequate filling of the bladder as determined by fluoroscopic criteria in 50 per cent of the patients. On the average 50 to 100 cc. of opaque material can be injected after flow has stopped by gravity pressure.

The injection of this additional material influenced the incidence of reflux. Fifty patients were observed in which the bladder was first filled by controlled gravity pressure and then followed by hand injection of enough additional opaque medium to meet the fluoroscopic criteria of adequate filling (Table II).

Thirty-one and 34 of the patients, respectively, showed reflux. Reflux is considered by most authorities as being abnormal.[3,7] The demonstration of reflux in 3 additional patients is significant and indicates the superiority of the fluoroscopic method of filling. The question: "Can reflux be produced by over-pressure in an otherwise normal genitourinary system?" is naturally raised. In our experience this does not occur with this method. In these particular patients it did not occur because one had a Hutch diverticulum, 2 had trabeculated bladders, and all had dilated tortuous ureters and pyelonephritis.

The fluoroscopic method of filling also ensures a higher number of adequate urethrograms, being 72 per cent and 94 per

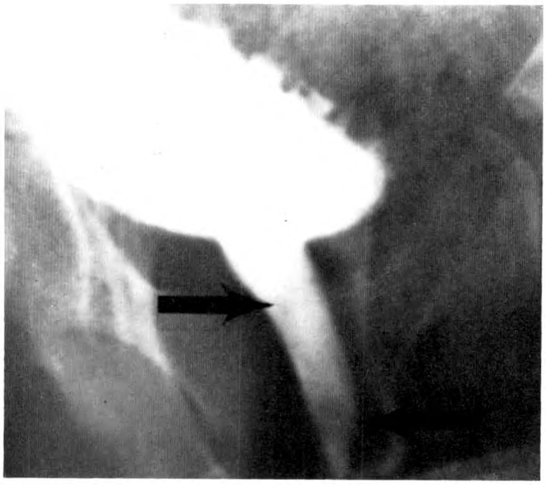

FIG. 5. Spot roentgenogram showing granulomatous defects in the urethra secondary to urethritis. These have been observed and studied only in females.

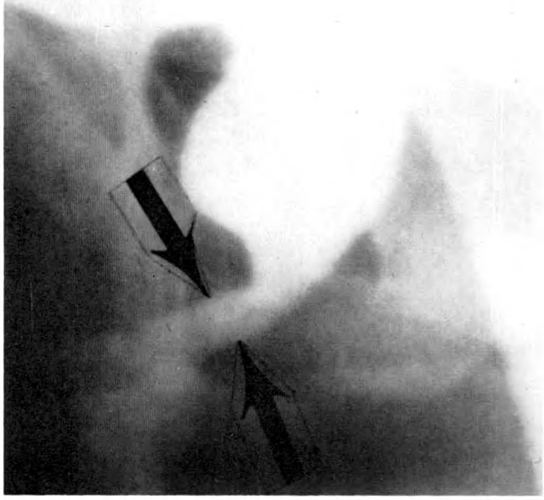

FIG. 6. Distal urethral stenosis as demonstrated by a spot roentgenogram. Urethra is dilated above the stenosis.

TABLE II

COMPARISON OF GRAVITY PRESSURE AND FLUOROSCOPIC FILLING OF BLADDER IN 50 PATIENTS

	Reflux		Adequate Urethrograms	
	No.	Per Cent	No.	Per Cent
Gravity Filling	31	62	38	72
Fluoroscopic Filling	34	68	47	94

cent for gravity and fluoroscopic filling, respectively (Table II). Inability of the patient to void in a continuous stream was the cause of the inadequate urethrograms with gravity filling of the bladder. Additional filling by the fluoroscopic method yielded adequate urethrograms in all but 3. Two of these had severely dilated ureters with marked ureteral reflux, and the bladder emptied itself largely into the ureters. The third was a 13 year old female with psychologic inhibitions, a problem common in this age group.

The fact that most radiology departments have facilities and equipment for taking, processing, and handling spot films is an important practical consideration. A conventional fluoroscope with a phototimed spot film device is the only roentgenographic equipment required. Image amplification and television monitoring are added but not essential requirements. Cineroentgenography, on the other hand, requires image amplification, special developing and projection apparatus, and filing and storage facilities, which are not available in all hospitals.

CONCLUSIONS

Cystourethrography is a special roentgenologic procedure which should be performed with fluoroscopic control of bladder filling and filming. Multiple phototimed spot films should be used to document and demonstrate pathologic physiology and anatomy. Widespread use of this method of cystourethrography will standardize methods and play an important role in advancing our knowledge of disease of the urinary tract.

SUMMARY

1. The spot film method of cystourethrography proved equal to the cine method in demonstrating ureteral reflux.

2. Spot film cystourethrography proved superior to cine cystourethrography in demonstrating pathologic anatomy.

3. Cystourethrography is a special roentgenologic procedure which should be performed with fluoroscopic control.

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POLYVIEW VOIDING CYSTOURETHROGRAPHY IN CHILDREN

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A SIMPLE filming technique for voiding cystourethrography in children has been developed and used at the University of Iowa Hospitals since October, 1964. The procedure has been termed polyview voiding cystourethrography. The filming sequence can be performed on any standard roentgenographic or urologic table equipped with a removable Bucky tray and an overhead roentgen-ray tube. The only special equipment needed is a serialographic tunnel (Liebel-Flarsheim Co.) which replaces the removable Bucky tray (Fig. 1 and 2).

Four $5\frac{1}{2}$ by 7 inch serial, oblique roentgenograms of the bladder and urethra are obtained during voiding, on a single 11×14 inch film (the "poly film"), with the cassette manually moved in the tunnel for the 4 exposure positions. With a modest amount of practice, a radiologic technician can easily perform the cassette-moving sequence while timing the exposures by watching the urinary stream as it exits from the urethral meatus (Fig. 3).

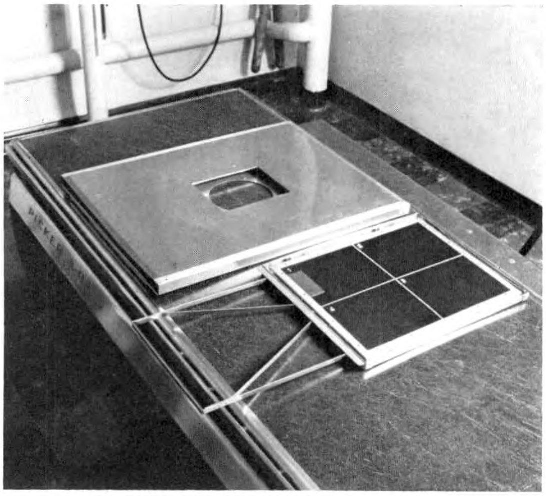

FIG. 1. Unassembled serialographic tunnel and tray containing numbered 11×14 inch cassette on top of a standard roentgenographic table.

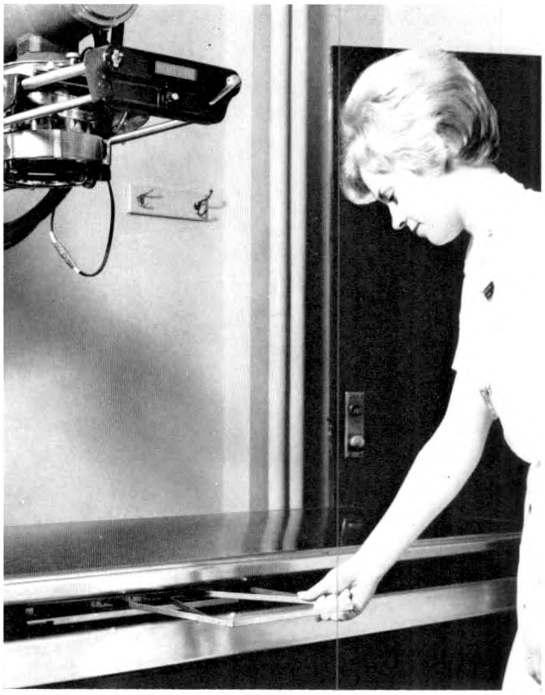

FIG. 2. Assembled tunnel and cassette tray in position, replacing the Bucky tray on a standard table.

The aim is to space the 4 exposures as uniformly as possible from the start to the finish of micturition. The exposures can be made by the technician who is moving the cassette if a foot switch is available, or a second technician can make the exposures on signal from the technician positioning the cassette. The shortest time interval in which 4 exposures can be made by this technique is about 5 seconds, thus making it possible to perform polyview voiding cystourethrography on any child over the age of about 6 months.

TECHNIQUE OF LOWER URINARY TRACT EVALUATION

In the roentgenographic diagnostic evaluation of children with urinary tract infection, our approach is as follows:

1. A supine preliminary roentgenogram

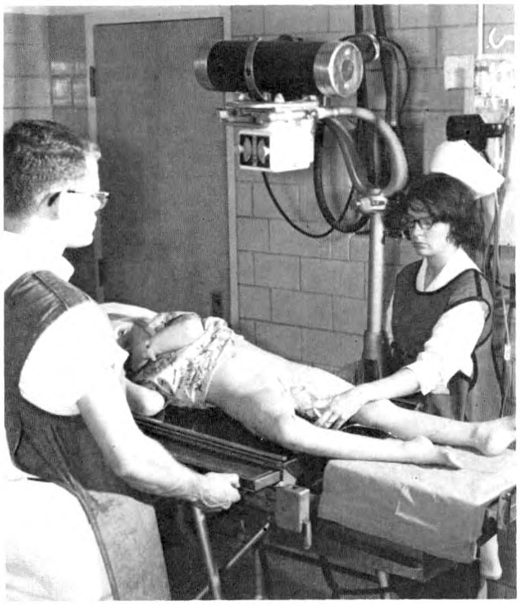

FIG. 3. Patient in oblique voiding position for polyview filming with tunnel in place on urologic table.

of the abdomen is obtained and checked for technical adequacy.

2. A small plastic catheter is placed in the urinary bladder and the residual urine is removed, the volume is recorded, and a specimen is obtained for cultures and urinalysis.

3. Twenty per cent methiodal sodium* in an intravenous bottle is allowed to flow into the bladder by gravity through plastic intravenous tubing attached to the catheter. The volume is determined by age and by signs of development of bladder distention.

4. A supine cystogram is obtained.

5. The patient is then placed in the left or right posterior oblique position (Fig. 3), the catheter is removed, and a voiding polyview filming is done.

6. A postvoiding abdominal roentgenogram is then obtained.

7. The roentgenograms are checked, and if excessive vesico-ureteral reflux is not present, intravenous urography is performed.

COMMENT

The role of voiding cystourethrography in the evaluation and management of urinary tract infections in children has been well established by the work of Burrows and Allen,[1] Davis *et al.*,[2] Kjellberg *et al.*,[3] and Tristan *et al.*[4] Their studies have been based on three methods of voiding cystourethrography: (1) multiple spot roentgenograms obtained at fluoroscopy (Burrows and Allen, Davis *et al.*); (2) serial filming on automatic cassette changers (Kjellberg *et al.*); and (3) cinefluorographic studies (Tristan *et al.*).

In the day-to-day practice of radiology, these techniques have limitations which have prevented the routine use of voiding cystourethrography by the practicing radiologist. These are: use of complicated, expensive equipment; excessive patient radiation exposure; quality of anatomic film detail; and presentation of roentgen evidence to the referring physician.

Use of automatic film changers immediately limits the procedure to a restricted number of larger hospitals and offices. In addition, the serial changers are expensive and are plagued by maintenance problems and frustrating breakdowns.

Fluoroscopic spot roentgenograms taken serially during voiding are simple to obtain but have the disadvantage of increased patient radiation dosage. Image intensifier usage has decreased radiation dosage but requires complicated expensive equipment. Adding cinefluorography to this method greatly increases dosage and complicates film processing and viewing.

The anatomic film detail obtained using an overhead tube and movable grid is superior to that of fluoroscopic spot roentgenograms. Detail in cine studies is not optimal due to inherent film limitations, and this technique is primarily of value for evaluation of dynamics of flow and not anatomic detail.

A polyview filming of the voiding sequence is the simplest method of presenting roentgenographic evidence to the referring physician. Fluoroscopic spot roentgenograms also have this advantage but are associated with increased patient radiation dosage. Multiple serial changer roentgenograms as a rule dismay everyone but the radiologist and are awkward to handle. Cine viewing is time consuming, requires special projection equipment, and often is difficult to arrange for the convenience of all concerned.

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Thus, polyview voiding cystourethrography has definite advantages over the above methods. It is easily performed with simple equipment, radiation dosage is low, anatomic film detail is good, and roentgenographic evidence is easy to present to the referring physician. Examples of polyview films are shown in Figures 4 and 5, and illustrate the roentgenographic findings in meatal stenosis and urethritis.

SUMMARY

Lower urinary tract infection in children is a relatively common clinical problem. Polyview voiding cystourethrography pro-

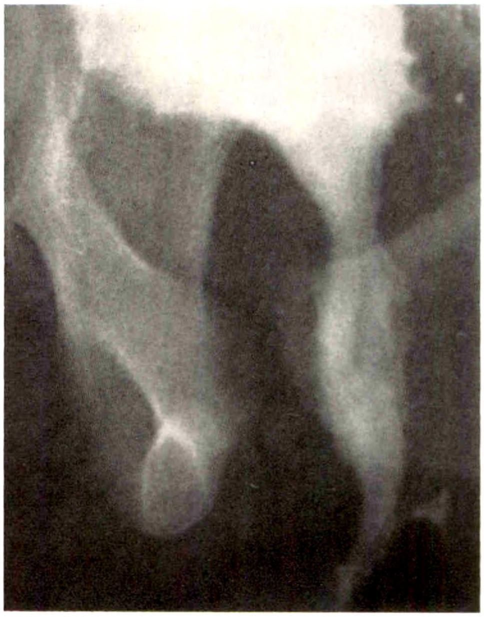

Fig. 5. Single frame from a polyview film showing urethral mucosal detail in a 3 year old girl with severe urethritis.

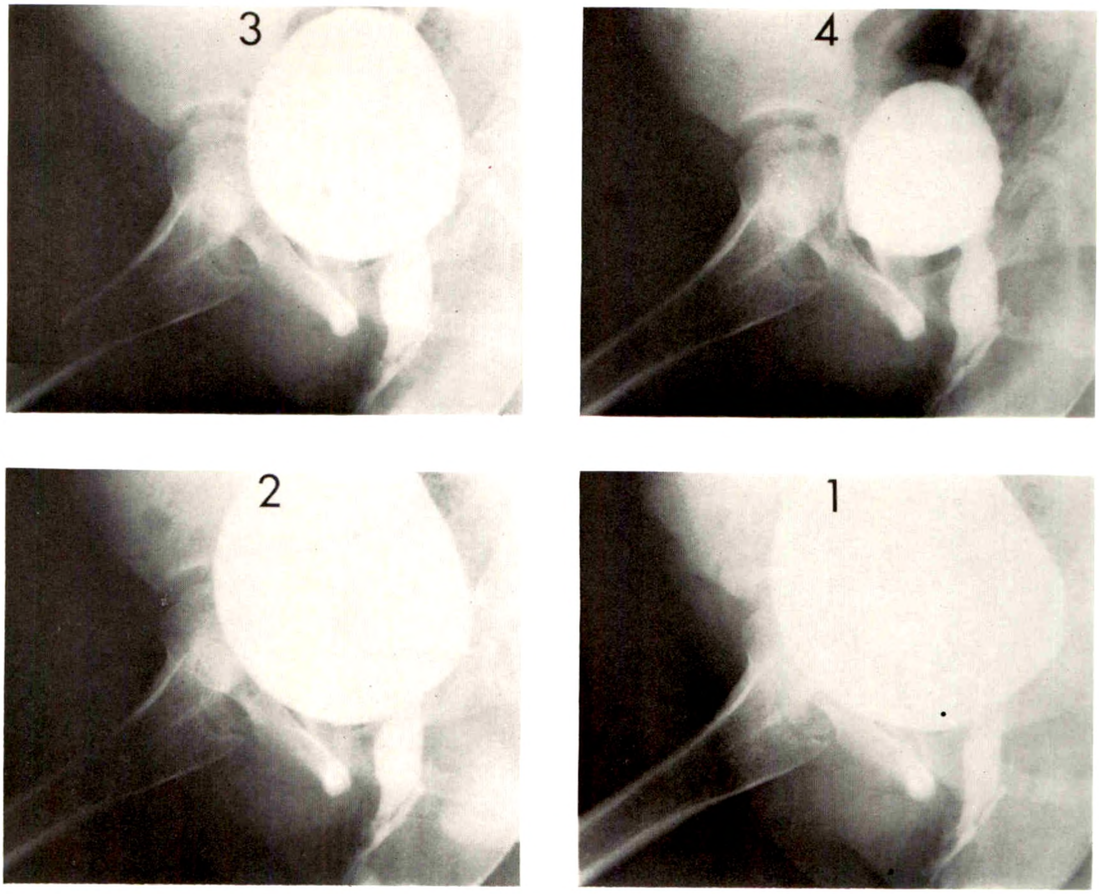

Fig. 4. Polyview film demonstrating meatal stenosis in an 8 year old girl.

vides a method for roentgenographic evaluation of the bladder and urethra that is technically simple and inexpensive, provides good anatomic film detail, and involves minimal patient radiation dosage. The details of technique are described.

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The technical assistance of Mr. Richard M. Feeney, R. T., was invaluable in establishing this as a practical roentgenographic procedure at the University Hospitals.

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RETAINED THORIUM DIOXIDE MEDIA IN SEMINAL VESICULOGRAPHY*

A FOLLOW-UP STUDY WITH DOSE ESTIMATES

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A COMPREHENSIVE review of the early use of thorium and other radioisotope materials in medicine and industry has been presented by Looney.[14] In 1928, thorium was first used clinically[17,19] to visualize the liver and spleen roentgenographically; it gradually became more widely used for that purpose[11,21] and as a contrast material for carotid angiography, bronchography and cerebral angiography.[14] It was also used in placentography, mammography, angiography of the extremities,[14] and to visualize genitourinary structures.[22] Later, it was reported useful in detecting accessory spleens.[18]

Initially, injections of medications into the vasa deferentia were made for the treatment of infections of the vasa and seminal vesicles.[2,3,4] Subsequently, a variety of compounds was used in attempts to visualize the seminal vesicles,[5] either by vasostomy or by instillation via a transurethral catheter with its tip in the ejaculatory duct. It was noted that such medications were not infrequently retained in these structures for more than 1 year.[5]

Other indications for seminal vesiculography were the visualization of structures in patients with aspermia but preserved testicular function; in adult candidates for orchiopexy; and in patients with post-herniorrhaphy pain.[5] With the introduction and subsequent increase in popularity of the thorium dioxide compounds as contrast media, they were found to visualize the genitourinary structures well, but some investigators cautioned against their use in seminal vesiculography and pyelography.[20,22]

In recent years, thorium dioxide-induced tumors have been reported with steadily increasing frequency. Most of these reports concerned individuals who received relatively large amounts of thorium dioxide intravenously, either for the visualization of the liver and spleen or certain vascular structures, particularly those of the cerebral circulation. These reports have substantiated laboratory investigations[25] in which a similar cause-effect relationship was demonstrated. It has been pointed out that any case with thorium retention should have a guarded prognosis and that the dose, no matter how small, is never to be considered innocuous.[1]

Thorium dioxide is also considered responsible for severe fibrotic reactions at the sites of injection, particularly in cases of extravasation.[1,7,27] In a number of instances, it has been responsible for tumors at injection sites.[6] Thorium dioxide-induced tumors have developed following intracavitary use and following procedures in which no significant retention of contrast material might be expected, such as retrograde pyelography, salpingography and dacryo-

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cystography. Dahlgren's[10] summary of some of these cases is shown in Table I.

A review of the Japanese literature suggests that thorium dioxide was infrequently used in Japan as an intracavitary contrast agent, but occasionally it was used intravenously, especially in hepatolienography and cerebral angiography. A number of cases of liver damage and neoplasms in or adjacent to the liver due to thorotrast injection are recorded in the Japanese literature.

Two cases have been reported by Nihira *et al.*[16] in which residual thorium dioxide was identified in tumors which developed following spermatocystography. However, the tumors were not identified as malignant. Yanagihara and Nishiyama[29] reported a 32 year old male in whom a mass was noted at the injection site 2 years

TABLE I

TUMOR DEVELOPMENT AFTER USE OF THOROTRAST[10]

Authors		Type of Tumor	Purpose of Injection	Dose (cc.)	Latent Period (yr.)	Sex	Age* (yr.)
Zollinger	1949	Spindle-cell sarcoma of kidney	Pyelography	30	16	M	64
Austoni	1950	Carcinoma of breast	Mammography	10	12	M	47
Ruf and Philipp	1950	Carcinoma of eyelid	Dacryocystography	—	35	M	51
Hofer	1952	Carcinoma of maxillary sinus	Maxillary visualization	—	10	F	64
Vogtlin and Minder	1952	Bronchogenic carcinoma	Bronchography	30	18	M	47
Gros *et al.*	1955	Carcinoma of maxillary sinus	Maxillary visualization	—	15	M	36
Scheibe	1955	Malignant peritoneal thorotrastoma	Intraperitoneal	24	17	F	60
Boemke	1956	Carcinoma of kidney	Pyelography	—	—	M	75
Budin and Gershon-Cohen	1956	Carcinoma of breast	Mammography	—	17	M	43
Federlin and Scior	1957	Carcinoma of ovary	Salpingography	—	23	F	45
Jacob and Schostok	1957	Carcinoma of kidney	Pyelography	—	25	F	49
Roth	1957	Bronchogenic carcinoma	Bronchography	—	13	M	38
Nielsen and Kracht	1958	Mixed tumor of kidney	—	—	—	F	66
Verhaak	1958	Adenocarcinoma of kidney	Pyelography	—	21	F	43
Verhaak	1958	Carcinoma *in situ* of kidney	Pyelography	—	23	F	44
Gelzer and Scheidegger	1959	Carcinoma of seminal vesicle	Urethrovesicography	—	14	M	68
Alken *et al.*	1960	Carcinoma of kidney	Pyelography	—	23	M	56
Cattell and Kahn	1960	Peritoneal carcinoma	Salpingography	—	21	F	48
Gros *et al.*	1960	Carcinoma of maxillary sinus	Maxillary visualization	—	14	F	49
Kligerman *et al.*	1960	Carcinoma of maxillary sinus	Maxillary visualization	—	18	F	32
Kligerman *et al.*	1960	Carcinoma of maxillary sinus	Maxillary visualization	—	21	M	39
Kligerman *et al.*	1960	Carcinoma of maxillary sinus	Maxillary visualization	—	10	M	70
Kligerman *et al.*	1960	Carcinoma of maxillary sinus	Maxillary visualization	—	15	F	70
Kruckemeyer *et al.*	1960	Carcinoma of kidney	Pyelography	—	23	F	45

* Age at diagnosis or death.

following seminal vesiculography. In this case the tissue was excised and particles of umbrathor were identified in a granulomatous lesion. By roentgenography, the same investigators also detected retained thorium dioxide in a seminal vesicle of a 30 year old male 9 years after seminal vesiculography.[29]

Since it is difficult to prove that a tumor has resulted from thorium dioxide administration, 3 basic criteria for establishing causal relationship have been advanced by Dahlgren.[10] The particles of the material must lie in the vicinity of the tumor; there must be a latent period sufficient for the development of a neoplasm; and the radiation dose to the tissue must be sufficient to produce neoplasm.

Two of the most widely used thorium dioxide preparations were thorotrast and umbrathor. Thorotrast is a colloidal suspension containing 25 per cent thorium dioxide and 20 per cent dextran with 0.15 per cent methyl-p-hydrobenzoate as a preservative.[9] Umbrathor is also a colloidal suspension of thorium dioxide, in 25 per cent concentration,[28] with a greater acidity, and reportedly outlines structures in better detail because of its flocculation on surfaces, especially in seminal vesiculography.[28]

A method of seminal vesiculography using thorium dioxide compounds in patients roentgenographed at the Atomic Bomb Casualty Commission (ABCC), Hiroshima, Japan, was previously reported.[28] In that study, patients with various clinical diagnoses were examined for possible abnormalities of the genitourinary structures. Small amounts of the medium were injected into the vasa deferentia by vasostomy at the Department of Urology, Hiroshima University Medical School. Five to 48 hours following injection, roentgenography was performed at ABCC.

MATERIAL

METHOD OF FOLLOW-UP

Because of the widespread interest in follow-up studies of all patients who have received injections of thorium dioxide and because the present series of patients represents a rather unique group who experienced seminal vasiculography with this medium, extensive efforts were made to contact and re-examine them. The method of contacting subjects examined regularly in the clinics of ABCC[15] greatly facilitated this follow-up study. A number of the subjects who received the examination were formerly members of the Japanese Armed Forces. Despite extensive efforts with the assistance of prefectural governmental offices and the Japanese Self-Defense Forces, some who had moved to distant parts of the country could not be located. Of the 56 cases examined by seminal vesiculography, 24 were again contacted and 23 examined. One patient refused examination because of undiagnosed illness. The lapse of time from seminal vesiculography to the present examination varied from 12 to 14 years.

The present examinations of these patients comprised a complete history, physical examination, routine laboratory studies, liver function tests, roentgenograms of the chest, abdomen and pelvis, including the genitalia, electrocardiograms, and other studies as indicated. No biopsy or surgical specimens were obtained.

There were 9 deceased patients in this follow-up study, none of whom were autopsied (Table II A). Three of the deceased were reported on death certificates as having neoplastic disease at the time of death. Case 1 died 5 months after seminal vesiculography, with a diagnosis of carcinoma of the urinary bladder. That diagnosis was established at the time of the initial examination. Case 2 also was diagnosed as having carcinoma of the urinary bladder at the time of seminal vesiculography, and died 7 years later; cause of death was reported as carcinoma of the urinary bladder. Case 3 had a prostatic tumor at the time of seminal vesiculography, and died 3 months later, reportedly of a "weak heart." No diagnoses of neoplasia involving the genitourinary system were made in the other deceased patients.

Table II B summarizes the results of the follow-up studies of 23 patients who are known to be alive.

Of the 23 cases studied, 14 had nodularity, swelling, fibrosis or induration at the sites of the injection near the vasa deferentia. Twenty-one cases showed a quantity of retained material near the injection sites, in the scrotum, or the regions of the epididymis and testis. Two cases had nodularity of the epididymis or seminal vesicles, but no retained contrast material was seen in these regions at this time by roentgenography. Nodularity in these locations, therefore, may not be due to the contrast medium. Nine cases showed no abnormality of soft tissue at or near the injection sites. In all but 2 cases, retained contrast material was detected roentgenographically.

ROENTGENOGRAPHIC APPEARANCE

The roentgenographic appearance of retained medium in 2 cases is shown in Figures 1, *A* and *B;* and 2, *A* and *B.* The

Table IIA

SUMMARY OF DISEASED PATIENTS
(9 cases)

Seminal Vesiculography							Deceased		
Case	Age	Clinical Diagnosis	Date	Medium			Date of Death	Death Certificate (cause of death *in italics*)	Remarks
				T/U	cc.				
					Rt.	Lt.			
*Case 1	57	Chyluria	2/22/51	U	1.5	1.5	7/10/51	*Tuberculous meningitis; miliary pulmonary tuberculosis*	Carcinoma of urinary bladder diagnosed in 1951
*Case 2	67	Bladder cancer	10/7/49	U	?	?	11/26/56	Onset of illness in 1949; *cancer of bladder*, duration about 7 years	
*Case 3	54	Cancer of prostate, chills, fever and pyuria	3/10/50	T	↑ 1.5 0.3 ↓	↑ 1.5 0.3 ↓	6/23/50	*Natural death; weak heart;* prostatic tumor, 1 year; metastases, 3 months	
Case 4	42	Impotence	2/27/50	T	2	2	5/17/50	*Toxemia due to hypnotic drug; neurasthenia*	
Case 5	27	Tuberculosis of kidney, bladder and prostate	6/23/50	T	1.7	1.7	10/2/50	*Tuberculous spondylitis; tuberculous meningitis*	
Case 6	61	Prostatic hypertrophy	2/26/50	?	?	?	8/4/52	*Pulmonary tuberculosis*	
Case 7	58	Benign prostatic hypertrophy	12/21/50	U	1.5	1.5	2/20/58	*Liver cirrhosis*	
Case 8	28	Chronic gonococcal urethritis	2/8/51	U	1.5	1.5	4/12/61	Cause of death unknown	
Case 9	54	?	10/12/50	?	?	?	9/11/54	*Cardiac weakness; uremia; amyotrophic lateral sclerosis; urethral stenosis*	

Note T = Thorotrast.
U = Umbrathor.
? = Unknown.
↑ = Proximal injection.
↓ = Distal injection.
Asterisks indicate cases previously reported.[28]

Table IIB

SUMMARY OF PATIENTS ON FOLLOW-UP EXAMINATIONS

(23 cases)

Seminal Vesiculography							Results of Follow-up Study						
				Medium					Vas				
					cc.								
Case	Age	Clinical Diagnosis	Date	T/U	Rt.	Lt.	Interval History	Physical Examination	Rt.	Lt.	Laboratory Studies	Roentgenography (retained medium)	Remarks
*Case 10	23	Ureteral stone; spermatocyst	10/ 7/49	U	?	?	Gastritis in 1962; urticaria	5×5 mm. nodule in right vas	1	0	Negative	Rt. vas: 4 mm. (×2) Lt. vas: 4 mm.	
Case 11	49	Acute prostatitis	12/ 7/50	?	?	?	Pulmonary tuberculosis 18 yr. ago; prostatitis with fistula 11 yr. ago with operation	Fibrosis: right vas 1×1 cm., left vas 5×5 mm.; swelling	2	2	Thymol turbidity 6.6, urine phosphate: 1+	Rt. vas: 5 mm. Lt. vas: 6 mm.	Scintillation counter study
*Case 12	71	Prostatic calculi	3/ 8/50	T	↑ 1.5 0.3 ↓	0 0	Bladder calculus in 1950; prostate surgery at same time	Arteriosclerotic fundi, systolic and diastolic murmurs, BPH with urinary retention, hypertensive cardiovascular disease as aortic insufficiency	0	0	Urinalysis: occasional trichomonas, 15–20 WBC, 5–8 RBC per high power field	Rt. vas: 20×60 mm. Lt. vas: 0	Prostatic calculi, scintillation counter study
Case 13	35	Operation for birth control	6/ 7/51	U	1.5	1.5	Vasectomy, 13 yr. ago; gastric ulcer 3 yr. ago	Negative	0	0	Negative	Rt. scrotum: 2 mm. Lt. scrotum: negative	
*Case 14	36	Tuberculous epididymitis	9/19/49	?	?	?	Pain; epididymitis in 1949; epididymectomy in Sept. 1949; postmicturition pain	Left inguinal scar, 1×1 cm. mass of right inguinal region for several years	1	0	Negative	Rt. scrotum: 5 mm. diameter	

Note: T=Thorotrast.
U=Umbrathor.
?=Unknown.
Asterisks indicate cases previously reported.[25]

↑ Proximal injection.
↓ Distal injection.

0=Normal.
1=Mass, nodularity
2=Fibrosis, induration.

TABLE IIB—(*Continued*)

Seminal Vesiculography							Results of Follow-up Study						
Case	Age	Clinical Diagnosis	Date	Medium			Interval History	Physical History	Vas		Laboratory Studies	Roentgenography (retained medium)	Remarks
				T/U	cc.								
					Rt.	Lt.			Rt.	Lt.			
*Case 15	58	Calculi in urinary bladder and prostate, spermatocyst	9/30/49	?	?	?	Operation for urinary bladder calculus in 1950	Cataracts, hypertension, penis shortened, scarred and hyperpigmented	0	0	Negative	Rt. vas: 1 cm. Lt. vas: 2–3 mm. Rt. testis: 2 mm. Lt. testis: 3 mm.	Aneurysm of thoracic aorta on chest roentgenogram
*Case 16	32	Impotence	10/14/49	U	?	?	?Cholecystitis in 1960; ?gastritis in 1963	Both testicles small, "pea size" bilateral swelling in vas	1	1	Alkaline phosphatase: 10.1	Rt. scrotum: 7 mm. (×2) Lt. scrotum: 4 mm.	
*Case 17	43	Chronic eczema	12/28/49	T	2	2	Generalized urticaria in 1936; in 1949 localized at scrotum; weight loss of unknown amount	Small nodules at anterior triangle neck, chronic bronchitis and emphysema	0	0	Hookworm ova in stool	Rt. vas: 1 mm.	
*Case 18	31	Prostatic tumor	3/10/50	T	↑ 1.5 0.3 ↓	↑ 1.5 0.3 ↓	Tuberculosis of urinary bladder 10 yr. ago; 40 injections of streptomycin	Nodularity at both vas injection sites, both vasa firm	1	1	Negative	Rt. vas: 1.5 mm. Lt. vas: 1.5 mm. Rt. testicle: 8 mm.	Pulmonary tuberculosis, minimal active
*Case 19	42	Cowperitis, prostatitis, swelling and pain in prostate	5/10/50	T	1.5	1.5	Spondylolysis in 1950?	Slight swelling at left vas posteriorly, spondylolysis?	0	1	Negative	Rt.: 0 Lt.: 0	Spondylolysis, contrast material in spinal canal, no retained contrast medium of seminal vesiculography
Case 20	39	Sterility	3/20/50	T	1.5	1.5	Bronchial asthma 1 month; pulmonary tuberculosis 1 yr.	Dyspnea, rales and fever, benign prostatic hypertrophy with obstructive uropathy, eighth nerve damage	0	0	WBC: 23,000 RBC: 3,190,000 Hb: 11.2 S.R.: 32 Th. Turb.: 11.4 CC Flocc.: +++	Rt. vas: 1 mm. Lt. vas: 0	Active pulmonary tuberculosis, chronic bronchiectasis, foreign body in abdominal wall

TABLE IIB—(*Continued*)

Seminal Vesiculography							Results of Follow-up Study						
Case	Age	Clinical Diagnosis	Date	Medium			Interval History	Physical History	Vas		Laboratory Studies	Roentgenography (retained medium)	Remarks
				T/U	cc. Rt.	cc. Lt.			Rt.	Lt.			
Case 21	20	Soft chancre, acute gonococcal epididymitis	6/12/50	?	?	?	Treatment for gonorrhea in 1950; bilateral ligature of vasa in 1960	Negative	0	0		Rt. scrotum: 1.5×2.0 mm. Lt.: 0	
Case 22	29	Acute gonococcal urethritis	6/21/50	T	1.5	1.5	Tuberculous epididymitis 12 yr. ago; epididymectomy; gastric ulcer in 1963	Borderline hypertension	0	0	Enterobius ova in stool	Rt. vas: 1 mm. Rt. scrotum: 1 mm.	
Case 23	21	Chronic gonococcal urethritis	10/10/50	U	1.5	1.5	Pulmonary tuberculosis at 22 yr. of age, with 1 yr. treatment	Indurated nontender vasa, both sides	2	2	Negative	Rt. vas: 4 mm. Lt. vas: 6 mm.	
Case 24	16	Chronic gonococcal urethritis	12/ 7/50	U	1.5	1.5	Contusion of right abdomen in 1956 with hematuria	Bilateral induration at vasa, nontender, postoperative disk syndrome, cervical osteoarthritis, ulnar neuritis	2	2	Urinalysis: 10–12 WBC per high power field	Rt. vas: 5 mm. Lt. vas: 13×4 mm.	
Case 25	26	?	11/ 7/50	?	?	?	7 kg. weight loss in 6 months	Varicocele in right testicle, hemangioma of right ear	0	0	Urinalysis: trichomonas	Rt.: 0 Lt.: 0	No retained medium, no recollection of seminal vesiculography
Case 26	25	Acute gonococcal urethritis	11/16/50	U	1.5	1.5	Pulmonary tuberculosis in 1954 with chemotherapy; appendiceal abscess in 1954	Right indurated seminal vesicle, right epididymis large and fibrotic, nontender	2	0	Negative	Rt. vas: 5 mm. Lt. vas: 0	Pulmonary tuberculosis, moderately advanced, probably active
Case 27	45	Chronic gonococcal urethritis	12/14/50	T	1.5	1.5	Liver disease in 1961 and 1963	Right cervical adenopathy, enlarged prostate, left varicocele, female escutcheon, chronic bronchitis, benign prostatic hypertrophy	0	0	RBC: 3,700,000 Hb.: 10.6 S.R.: 28 Total Prot.: 6.7 Alb.: 3.0 Glob.: 3.7	Rt. vas: 2×6 mm. Rt. scrotum: 2 mm. Lt.: 0	Bullous emphysema, atelectasis

TABLE IIB—(*Continued*)

Seminal Vesiculography							Results of Follow-up Study						
Case	Age	Clinical Diagnosis	Date	Medium			Interval History	Physical History	Vas		Laboratory Studies	Roentgenography (retained medium)	Remarks
				T/U	cc. Rt.	cc. Lt.			Rt.	Lt.			
Case 28	61	Prostatic hypertrophy	12/21/50	U	1.5	1.5	7 kg. weight loss in 6 months; suprapubic pain; pulmonary tuberculosis in 1957	Subcutaneous bitemporal nodules, abdominal 8×2 cm. mass, induration of both vasa	2	2	S.R.: 23 Urinalysis: 10–15 WBC 1–2 RBC per high power field	Rt. vas: 1 mm. Lt. vas: 5 mm.	Pulmonary tuberculosis, minimal, with questionable activity
Case 29	32	Tuberculous epididymitis	1/18/51	U	1.5	1.5	Pulmonary tuberculosis	Mass in left seminal vesicle, left varicocele	0	2	RBC: 3,900,000 Hb.: 11.5 S.R.: 29 Total Prot.: 7 Alb.: 3.9 Gob.: 3.1 Urinalysis: 90–120 WBC per high power field	Rt. vas: 10 mm. Lt. vas: 10 mm.	Staghorn calculus of left kidney
Case 30	32	Tuberculous vesiculitis, tuberculous epididymitis	2/ 8/51	U	1.5	1.5	Tuberculous orchitis in 1951 with orchidectomy; occasional opaque urine	Left testis retracted, "pea-size" swelling at right vas injection site	1	0	Negative	Rt. vas: 0 Lt. vas: 8 mm.	
Case 31	34	Spermatorrhea	3/ 8/51	U	1.5	1.5	Recent 5 kg. weight loss; easy fatigability	Small firm nodule at right vas, right inguinal nodularity 1×1 cm.	1	0	Urinalysis: 2–6 RBC per high power field	Rt. vas: 5 mm. Lt. vas: 10 mm.	
*Case 32	20	Syphilis	6/ 9/49	U	2	2	Duodenal ulcer in June 1964	Hepatomegaly, small nodularity in both vasa, scar in right inguinal area	1	1	Negative	Rt. scrotum: 11×5 mm. Lt. scrotum: 4 mm.	Duodenal ulcer deformity on gastrointestinal series

distributions of contrast material in Case 10 and Case 11 were typical for most of the patients in this series. Figure 1*A* shows the distribution in Case 10 of the material at initial examination (1949) and Figure 1*B* at the present time in regions of the vasa deferentia injection sites.

A scintillation counter was used to detect activity over one deposit in Case 11. A comparison of these values with those of thorium dioxide standards in phantom material was made as shown in Table III.

Case 12 was of special interest because of a relatively large amount of contrast material visible around the right vas deferens and surrounding tissue. This 85 year old male had a clinical diagnosis of prostatic calculus at the time of seminal vesiculography in March, 1950, and excretion of a bladder calculus following a cystoscopic procedure which preceded the vesiculography by 1 week. At seminal vesiculography, only the right side was injected, and an unusual pattern was noted about the seminal vesicles at roentgenography. Figure 2*A* shows the roentgenogram made at the time of that procedure (1950) and Figure 2*B* the appearance at the present examination.

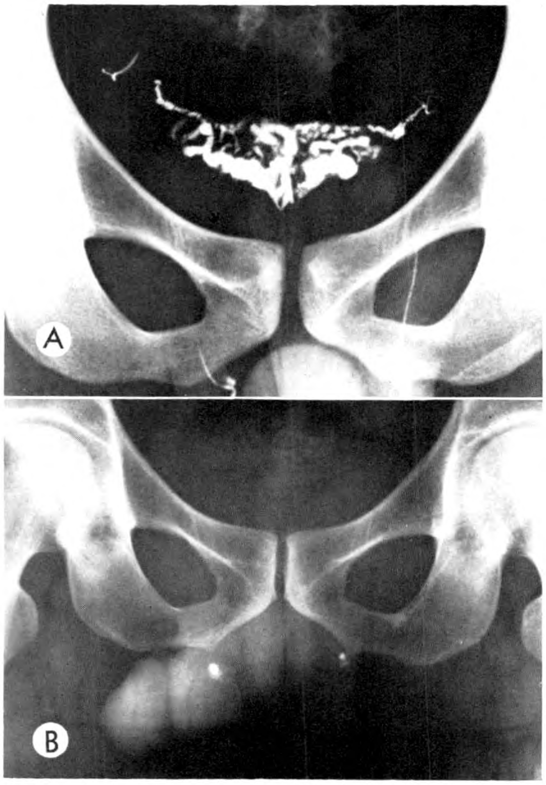

Fig. 1. Case 10. (*A*) Distribution of contrast material on seminal vesiculogram. (*B*) Follow-up examination.

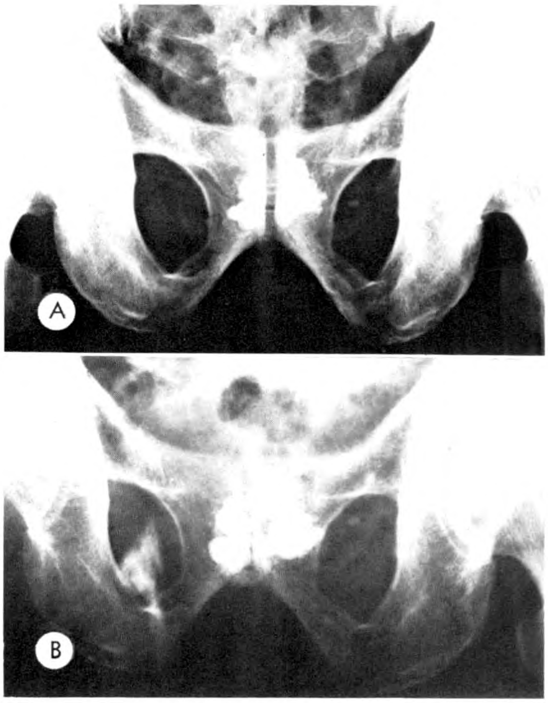

Fig. 2. Case 12. (*A*) Distribution of contrast material on seminal vesiculogram. (*B*) Follow-up examination.

This patient was examined again in June, 1963, and the history revealed that gonorrhea was contracted at the age of 24 years. He recalled prostatic surgery in March, 1950. Positive genitourinary findings on physical examination were a prostate gland 2 times normal size with nodularity in its right and left lobes, a right inguinal hernia and left orchidectomy. The urinary bladder was palpable 2 finger-breadths above the symphysis pubis. Clinical diagnosis was benign prostatic hypertrophy with urinary retention. On roentgenography, the contrast material in the soft tissues on the right side measured 2.5×6 cm. in the anteroposterior and 1 cm. in thickness in the lateral projection.

To determine whether any of the midline

TABLE III

VALUES OBTAINED USING SCINTILLATION COUNTER

	Contrast Material	Total cpm	Back-ground cpm	Net cpm
Patient Case 11	Right vas deferens	2,137	2,025	112
Thoro-trast Standard	0.2 ml.	2,425	2,305	120
	0.4 ml.	2,880	2,305	575
	0.6 ml.	3,149	2,305	844

density was due to retained contrast medium, a scintiscanner with a 1.5 inch diameter crystal was used with lead shielding over the right inguinal density. No activity was evident in the region of the midline density, which was, therefore, attributed to prostatic calcification. On removal of the inguinal shielding, an activity pattern of retained material on the right side was not established on the scintigram but was evident by the counting procedure. There having been no subsequent injections, thorotrast in the region of the prostate and seminal vesicles at seminal vesiculography may have subsequently migrated proximally and extravasated.

DOSE ESTIMATES

It is notoriously difficult to calculate dose to the tissues in which thorium dioxide media have been deposited, even when tissue specimens are available for analysis. The distribution of the material, the distribution and excretion of thorium daughters formed in the body, the excretion of thorium as a function of time following injection, the self absorption of particle energy within the deposits of thorium,[7,23,24,26] as well as the elapse of time from death to the removal of specimens from the cadaver,[18] all are important factors in these calculations.

Since we were unable to obtain biopsy specimens in this series of cases, one of us (H.Y.) estimated the dose in 2 cases, based on scintillation counting and densitometry techniques. On roentgenography, 1 of these (Case 11) exhibited retained contrast material in a distribution typical for the group; the other (Case 12) appeared to have a relatively large amount of material in the right inguinal region. Using the methods described in the *Appendix* to this article, the dose in Case 11 was 1.7×10^5 rem to each inguinal region. In Case 12, the right inguinal region was calculated to have received 1.0×10^5 rem.

DISCUSSION

On roentgenographic examination, 20 of the 23 patients examined in this follow-up study had evidence of thorotrast or umbrathor in or near the structures of the genital tract at one or more locations, in most cases at the sites of injection. In nearly all cases, the injection of 0.5–2.0 cc. of the material into each vas deferens was documented. In each case most of this quantity was subsequently excreted, and the amounts of residual material present after 12–14 years appeared to be small.

Latent periods of 10–35 years have been reported in most cases of thorium dioxide-induced tumors. In this study, no instances of neoplasm were attributable to the use of medium containing thorium dioxide. Nodularity at the sites of injection was presumably due to fibrosis and granulomatous reactions, similar to findings described in other reports. Presumably, these changes are the result of the radioactive properties of the material, rather than due merely to a foreign body reaction.[1] It is problematic whether this point could have been clarified even if biopsy material had been obtained in these cases.

Despite the fact that errors are inherent in calculating dose from such retained radioactive material, estimates were made for 1 patient who showed a roentgenographic pattern of contrast material typical for the group, and for another in whom a considerably greater quantity of material was apparent in the region of an injection site.

By using a scintillation counter, the activity detected in 1 of the patients with a typical amount of retained material on roentgenography approximated 0.8 cc. thorotrast. On this basis, it is estimated that no more than this amount is likely to be present in each inguinal region of the patients in this series.

Subcutaneous administration of thorotrast in laboratory animals has induced neoplasia, and neoplasms have resulted following extravasation and retention of such material from clinical use. It has been suggested that small amounts of thorium dioxide in tissue may require longer latent periods for the development of neoplasms.[8] Since patients often may not live through the latent period required for the development of neoplasms secondary to the administration of medium containing thorium dioxide, some of the neoplasms which develop may escape detection. Therefore, future periodic examinations of the individuals in this study would seem to be indicated. The recent contacting of these patients and the preliminary data may facilitate the future examination of this group.

SUMMARY

A brief review of the English and Japanese literature as to the past use of thorium dioxide-containing media is presented. Physical and laboratory findings including roentgenography in a follow-up study of 23 cases which received such contrast material for seminal vesiculography 12–14 years previously are also presented. Dose estimates were made for 1 patient typical of the entire group, and for another with a relatively larger residuum. Small amounts of retained contrast material were evident in all cases, but no case of neoplasia attributable to the presence of the medium was detected.

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The special efforts of the Department of Medical Sociology, ABCC, and members of its contacting staff are greatly appreciated. Grateful acknowledgement is also extended to Mr. Masayoshi Mizuno and Mr. Tatsuo Mandai and to members of the Research Institute for Nuclear Medicine and Biology, Hiroshima University for their assistance in the technical procedures employed in dose calculations.

APPENDIX

DOSE ESTIMATES

Densitometry method. An unopened quantity of the original thorotrast employed for seminal vesiculography in these patients (Thorotrast, Heyden Chemical Corporation, New York; 12 cc. vials, lot #172-1) was used to estimate the quantity retained and dose received in 2 patients.

To correlate optical density and thorium dioxide content and to establish the minimum density of contrast material detectable by roentgenography, serial dilutions were made from 2 cc. of thorotrast to 50 per cent, 25 per cent, 12.5 per cent, 6.2 per cent, 3.1 per cent and 1.5 per cent concentrations in small plastic cups. These were placed in a plastic tray permitting immersion into water phantoms for roentgenography.

Using phantoms 5, 10 and 20 cm. thick, roentgenography was performed at 100 kv., 100 ma., 1/10 second, with 2.5 mm. added aluminum filtration—the average factors employed in the follow-up examination of these patients—with the long axis of the tray at right angles to the roentgen-ray tube axis to minimize the anode effect. The 6.2 per cent dilution of the thorotrast was detectable using the 20 cm. water phantom.

Optical density (O.D.) of the contrast material on roentgenographic film was determined using a Macbeth-Ansco Color Densitometer, Model 12, and values were plotted against concentration as shown in Figure 3. These values are used to estimate the quantity of retained material evident on roentgenograms of the patients.

Some inaccuracy is inherent in the procedure due to dispersion of retained material in soft tissue, the variation in soft tissue thickness, and roentgenographic techniques. However, dose calculations

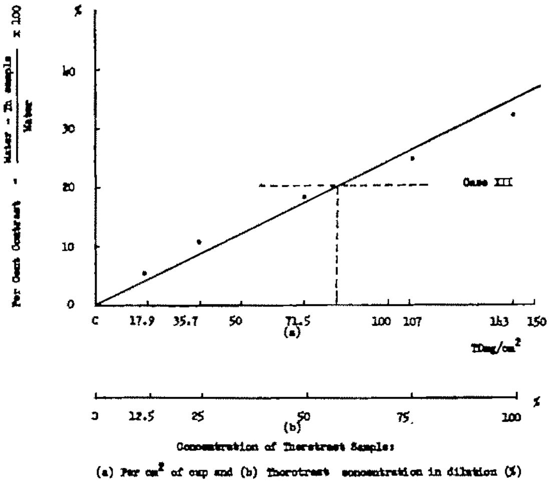

Fig. 3. Per cent contrast-thorotrast sample concentration curve. (Obtained by radiography of serial dilution standards of thorotrast.)

were made for Case 11, which showed a roentgenographic distribution of retained material typical for the group in the follow-up study, and Case 12 had a relatively large amount of material in the right inguinal region.

Concentration of the thorium dioxide (TD) standard was determined as follows:

Volume of solution (V): 2.0 cc.

Cross section area of cup (s): 3.5 cm.^{2}

Thorium dioxide concentration of 100 per cent thorotrast solution (c): 250 mg./cc.

Quantity of thorium chloride in the 100 per cent thorotrast solution, per cm.^{2} (d)

$$d = \frac{cV}{s} = \frac{250 \times 2.0}{3.5}$$

$$d = 143 \text{ mg.TD/cm.}^2 \text{ of cup.}$$

Per cent contrast of sample cup was calculated from the values in Figure 3 as follows:

Per cent contrast of D in base D_0

$$[\text{P.C.}] = \frac{D_0 - D}{D_0} \times 100\ (\%)$$

Concentration	Thorotrast Sample O.D.	Water O.D.	Per Cent Contrast of Sample	Thorium Dioxide mg./cm.^{2} (cup)
100%	0.68	1.03	34.0	143
75%	0.77	1.03	25.2	107
50%	0.83	1.03	19.4	71.5
25%	0.91	1.03	11.6	35.7
12.5%	0.97	1.03	5.8	17.9

Using the formula,

$$\frac{\text{O.D. Patient's left side} - \text{O.D. Patient's right side}}{\text{O.D. of left side}} = \%\ \text{contrast}$$

per cent contrast for the optical densities in these 2 patients was calculated as follows:

Case 11

$$\frac{(2.07 - 1.66)}{2.07} \times 100 = 20\%$$

Case 12

$$\frac{(1.37 - 1.09)}{1.37} \times 100 = 20.5\%$$

Quantity of thorium dioxide per square centimeter for each patient was estimated from the per cent curve (Figure 3) as follows:

Case 11	Case 12
80.0 mg./cm.^{2}	82.0 mg./cm.^{2}

Using millimeter-square-ruled paper, the area of each deposit of contrast material was calculated for each patient, 0.16 cm.^{2} and 2.88 cm.^{2}, respectively.

Total quantity of thorium dioxide was calculated as the product of area and density.

Case 11

$$80.0 \times 0.16 = 12.8 \text{ mg.TD}$$

Case 12

$$82.0 \times 2.88 = 236 \text{ mg. TD}$$

In Case 12, a thickness of 1 cm. was determined in lateral projection. The thickness of the retained medium in Case 11 was estimated to be 0.5 cm.

The volumes obtained were as follows:

Case 11	Case 12
0.08 cm.^{3}	2.6 cm.^{3}

From the effective absorptive energy for the tissue of reference[12] for thorium and its daughters, the dose was calculated according to the following formula:

$$R(\text{rem}) = \frac{(\text{disintegrations/sec.}/\mu\text{c}) \quad \begin{pmatrix}\text{effective}\\ \text{energy}\end{pmatrix} \quad \begin{pmatrix}\mu\text{c thorium}\\ \text{per organ}\end{pmatrix} \quad \begin{pmatrix}\text{time}\\ \text{in sec.}\end{pmatrix} \quad \left(\frac{\text{erg/mev.}}{100}\right)}{\text{organ weight* in grams}}$$

For each of these cases, dose was calculated as follows:

Case 11

$$R = \frac{3.7 \times 10^4 \times 41 \times 0.0014 \times 4.2 \times 10^8 \times 1.6 \times 10^{-8}}{0.08}$$

$$= 1.7 \times 10^5 \text{ rem.}$$

Case 12

$$R = \frac{3.7 \times 10^4 \times 41 \times 0.026 \times 4.18 \times 10^8 \times 1.6 \times 10^{-8}}{2.6}$$

$$= 1.0 \times 10^5 \text{ rem.}$$

Scintillation counting method. To verify the results obtained in Case 12, activity was measured over the right inguinal region using a scintillation counter (Atomic, Model 1016A) with a 1½ inch by 1 inch NaI crystal (photomultiplier voltage: 900 volts; discriminator control: 10; crystal-skin distance: 5 cm.). The phantom with the known quantity of standard thorotrast was measured under the same conditions. The values obtained were:

Phantom + 0.4 cc. thorotrast solution: 12,396 counts/5 min.
Phantom only: 11,054 counts/5 min.
Net counts for thorotrast solution: 1,342 counts/5 min.
268 counts/1 min.

Case 12

Right inguinal: 13,592 counts/5 min.
Left inguinal as control (background): 10,752 counts/5 min.
Net counts, retained medium: 2,840 counts/5 min.
568 counts/1 min.

The quantity of thorium dioxide retained in the patient was calculated as follows:

$$0.4 \text{ (cc.)} \times \frac{568 \text{ (cpm)}}{268 \text{ (cpm)}} = 0.85 \text{ (cc.)}$$

$$= 213 \text{ mg.TD}$$

$$= 0.023\ \mu\text{c thorium}$$

Using the same formula:

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* Estimated weight of tissue containing thorium dioxide medium.

$$R(\text{rem}) = \frac{(\text{disintegrations/sec./}\mu\text{c})\ \ (\text{effective energy})\ \ (\mu\text{c thorium per organ})\ \ (\text{time in sec.})\ \ \left(\frac{\text{erg/mev.}}{100}\right)}{\text{organ weight* in grams}}$$

$$R(\text{rem}) = \frac{3.7 \times 10^4 \times 41 \times 0.023 \times 4.18 \times 10^8 \times 1.6 \times 10^{-8}}{2.6}$$

$$= 9 \times 10^4 \text{ rem.}$$

The dosimetry calculations were made as a substitute for chemical analysis, since no biopsy material was available. The method necessarily incorporated some approximations such as phantom thickness, and the shape and volume of retained material. In the densitometric method an estimate was made of milligrams (microcuries) of thorium dioxide, whereas in the scintillation method radioactivity was used for estimating dose. It has been pointed out that, due to the effects of metabolism, the daughters and the parent material achieve equilibrium only after removal from the body.[18] This lack of equilibrium was not considered in calculating dose by the scintillation method. Even so, the results obtained by the 2 methods were approximately the same.

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* Estimated weight of tissue containing thorium dioxide medium.

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TESTICULAR TUMORS*

AN ANALYSIS OF 112 CONSECUTIVE CASES

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THIS study is a review of all patients with testicular tumors treated at the University of Wisconsin Hospitals between January 1, 1940 and December 31, 1960.

The records of 115 consecutive patients were analyzed. The histologic diagnosis was available in 112 cases; the 3 remaining patients entered the hospital with diffuse metastases from obvious testicular tumors and biopsy was not obtained. There were 96 patients who were treated before 1959 and therefore available for assessment of the 5 year survival rate. Histologic slides were obtained from 85 cases for a second review by the University Hospital pathologist, Dr. W. H. Jaeschke. In 20 additional cases the histologic diagnosis had been made by pathologists at the State Laboratory of Hygiene. Seven slides had been interpreted by practicing pathologists.

Initial surgery, consisting of orchiectomy, had been performed in 50 cases at the University of Wisconsin Hospitals while the remaining patients had been operated on by referring physicians. One patient, lost to follow-up, was considered dead as of the date of the last examination. He had a Stage 1 seminoma and was well when last seen, 3 months after treatment.

PATHOLOGY

The tumors were grouped according to the classification of Dixon and Moore[18] into 2 general categories:

(A) The germinal tumors arising from germinal epithelium.

(B) The nongerminal tumors arising from other testicular tissues.

(A) THE GERMINAL TUMORS

In the germinal tumors, 4 main histologic patterns were recognized (Fig. 1:)

1. The pure *seminomas* (Fig. 2 and 3) composed of large uniform cells with clear cytoplasm with or without a lymphoid stroma. There were 47 patients in this group (Group I).
2. The *embryonal carcinomas* (Fig. 4 and 5) composed of undifferentiated, totipotential germ cells which might undergo differentiation in various directions. Thirty-six patients were in this category (Group II).
3. The *teratomas* (Fig. 6) representing further differentiation of embryonal tumors into recognizable fetal or adult tissues. Two subgroups were identified: (a) teratomas with or without seminomatous elements (8 patients) (Group III) and (b) teratomas with either embryonal or choriocarcinomatous elements or both and with or without seminomatous tissues (9 patients) (Group IV).
4. The *choriocarcinomas* (Fig. 7) with both cytotrophoblast and syncytial trophoblast in villus-like arrangement (4 patients) (Group V).

These four characteristic histologic patterns were found alone or in combination with each other. The pure seminoma, characterized by extreme radiosensitivity, carried a relatively good prognosis, but when mixed with other types, had no influence on the course of the more malignant neoplastic process.

(B) THE NONGERMINAL TUMORS

In this category (8 patients), there were 2 reticulum cell sarcomas and 1 each of the following histologic varieties: fibrosarcoma, undifferentiated giant cell tumor (Fig. 8), interstitial cell tumor (Fig. 9), malignant

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† American Cancer Society Fellow in Radiology, July 1, 1963–June 30, 1964.

mesothelioma (Fig. 10), Brenner tumor (Fig. 11) and an unclassified tumor (several workers have suggested granulosa cell carcinoma) (Fig. 12). The 2 latter were of special interest because no case of Brenner tumor was found and only 2 reports describing granulosa cell types of testicular tumors were encountered in the available literature.[10,17] These 2 cases are therefore reported briefly.

Case I. A 67 year old male was admitted with a 40 year history of inguinal hernia. Four weeks prior to admission he noted swelling of the scrotum on the same side. The testis was found to be enlarged to 4 times the normal size and stone hard. An orchiectomy was done and the histologic appearance was consistent with that of a Brenner tumor (Fig. 11). There was no recurrence of the testicular tumor. Three years later the patient developed a squamous cell carcinoma of the larynx and expired, 8 years after the orchiectomy, from the laryngeal carcinoma.

Case II. A 50 year old male was admitted in 1958 with a 4 month history of left testicular enlargement. The testis measured 6×12 cm. and was hard and smooth. No feminizing features were present. Orchiectomy was done and the tumor was found to have metastasized to the spermatic cord. Postoperative radiation therapy was given with a dose of 2,000 r to the periaortic and inguinal areas over a 2 week period. To several workers the microscopic appearance suggested granulosa cell carcinoma (Fig. 12). The patient expired 2 months later from generalized metastases.

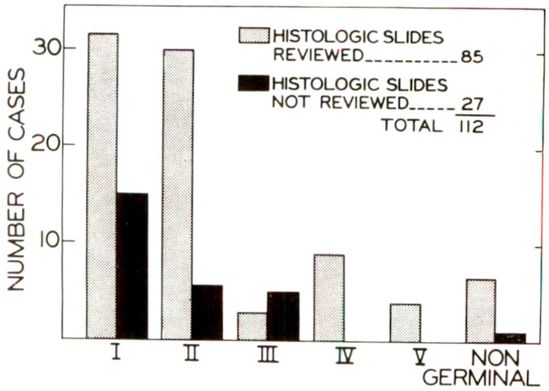

Fig. 1. Pathological grouping of 112 cases of testicular tumors. Germinal tumors: seminomas, Group I; embryonal carcinoma, Group II; teratomas (a) with or without seminoma, Group III; teratomas (b) mixed, Group IV; choriocarcinomas, Group V; and nongerminal tumors.

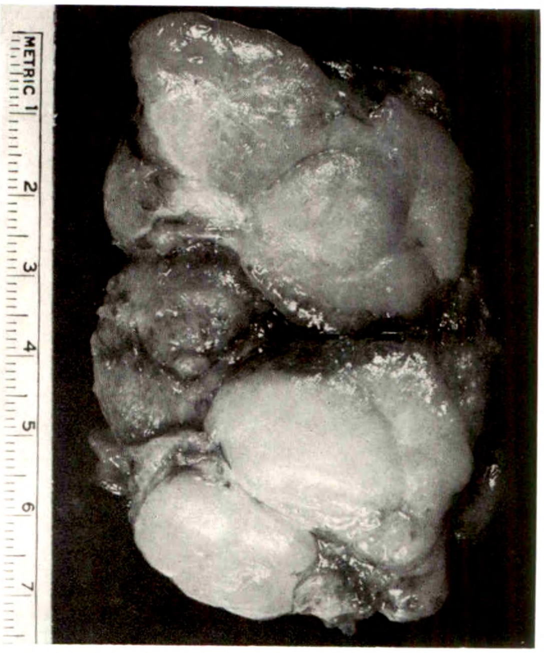

Fig. 2. Fleshy pale gray seminoma largely replacing testicular substance. These tumors usually comprise about 40 per cent of all the germinal tumors. They may reach quite large dimensions and also develop as discrete nodules in other histologic tumor types.

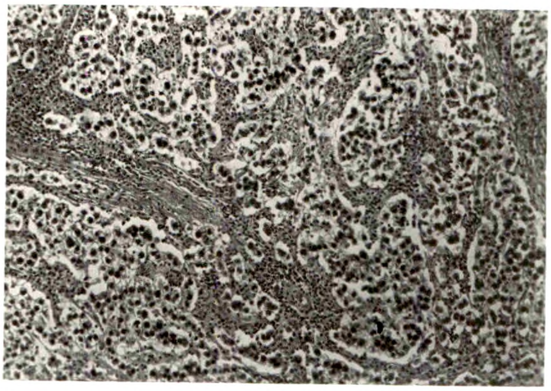

Fig. 3. Pure seminoma (73×). This tumor is composed of small, partly vacuolated polyhedral cells with prominent nuclei and centrally positioned nucleoli. Note the fine connective tissue septa, finely dotted with numerous lymphocytes.

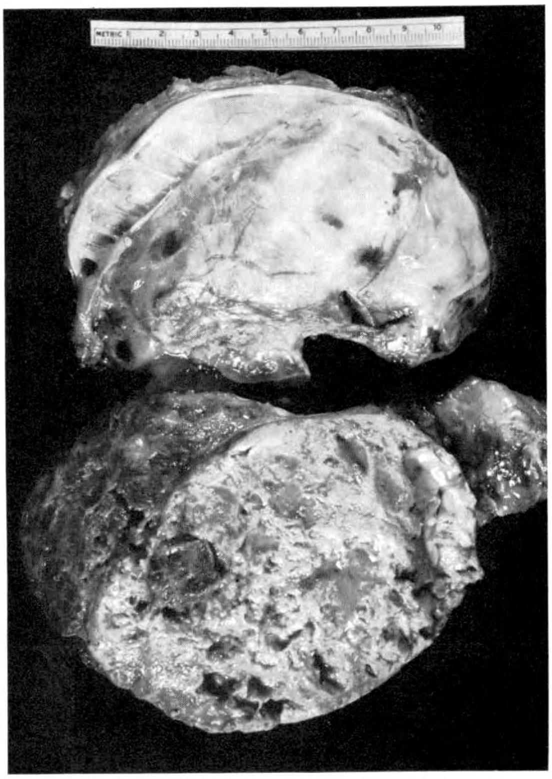

FIG. 4. Large, partly necrotic and hemorrhagic embryonal cell carcinoma of the testicle. These tumors usually comprise about 30 per cent of all germinal tumors. Discrete nodules of seminomatous elements may coexist.

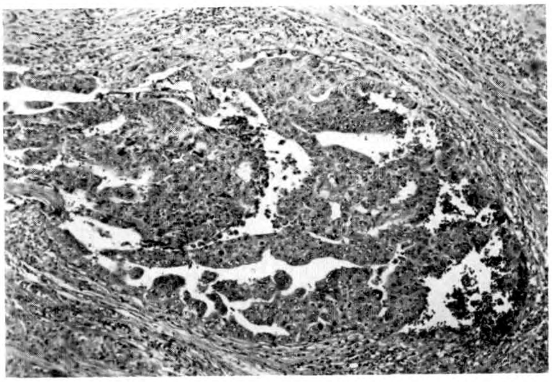

FIG. 5. Pure embryonal cell carcinoma (73×) composed of irregular sheets and anastomosing columns of neoplastic cells. These cells have a moderate amount of cytoplasm and prominent nuclei, as well as nucleoli. Mitotic figures are common. These tumors consist of highly malignant, multipotential cells which may be entirely undifferentiated or may show slight differentiation toward somatic or trophoblastic forms.

CLINICAL STAGES

The patients were separated into 3 clinical stages based on the anatomic extent of the disease:[4,45] Stage I comprised cases with tumor limited to the testis; Stage II those with metastases to retroperitoneal, iliac or inguinal lymph nodes, scrotum or spermatic cord; and Stage III those with metastases beyond the periaortic lymph nodes; *e.g.*, mediastinum, supraclavicular lymph nodes, bones, lungs, pleura, liver or other viscera. There were 72 patients in Stage I, 21 in Stage II and 19 in Stage III (Fig. 13). As might be expected, a relatively high proportion of the seminoma cases (70 per cent) was classified as Stage I, although it should be realized that this classification was on the basis of clinical examination alone—obviously a very inaccurate means for diagnosing metastatic involvement of

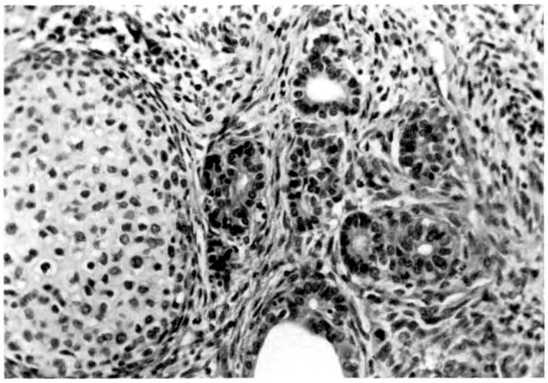

FIG. 6. Malignant teratoma with elements of nephroblastoma (170×). This view shows the oval plaque of cartilage and supporting stroma composed of spindle-shaped cells with prominent nuclei. Very occasional cells are in mitosis. Tubular structures composed of cuboidal and low-columnar cells with prominent nuclei are noted, but show little variation from one another. No rhabdomyoblasts are identified with certainty. Teratomas comprise usually about 30 per cent of all germinal tumors. The essential elements are made up of somatic tissues corresponding to either fetal or adult stages of development. Some teratomas may contain smooth muscle, nerve tissue and gastrointestinal or respiratory epithelium. These tumors may develop as pure teratomas or with admixture of seminoma (Group III) or with embryonal carcinoma, choriocarcinoma or both and with or without seminoma (Group IV).

retoperitoneal lymph nodes. Recently, lymphography has been of considerable value in the diagnosis of hidden retroperitoneal metastasis (Fig. 14).

Among the embryonal, teratomatous and choriocarcinomatous tumors, there was a proportionately larger number of cases classified as Stage II and III.

AGE

The average age at the time of diagnosis was 37 years with the youngest patient being 14 months and the oldest 80 years of age (Fig. 15). The germinal tumors occurred relatively early, the patients averaging between 29 and 39 years of age. The seminomas occurred slightly later (average age 39 years with a range from 8 to 55 years) than the embryonal carcinomas (average age 33 years with a range from 14 months to 52 years).

The nongerminal tumors usually occurred in older patients (average age 50 years).

SYMPTOMS AND SIGNS

By far the most common initial sign was enlargement of the testicle, encountered in 98 cases. Only 15 patients complained of pain in the testicle; a more common complaint was a feeling of heaviness in the scrotum. Pain in the groin or abdomen was recorded in 16 cases. There were initial

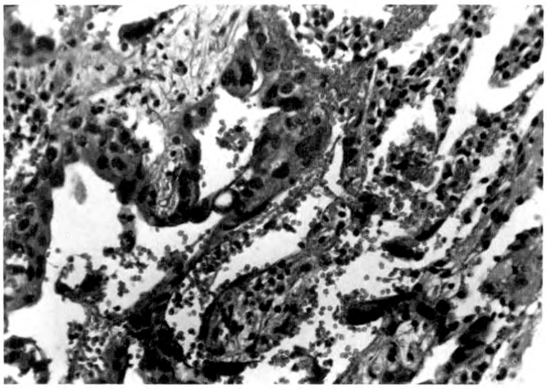

FIG. 7. Pure choriocarcinoma (170×). There is hemorrhagic, focally necrotic tissue with irregular cytoplasmic structures, and multiple nuclei of different sizes. These tumors usually comprise only 1 per cent or less of the germinal tumors and may exist with either seminomas or embryonal carcinoma or both. The essential element is the cytotrophoblast and the syncytial trophoblast in villus-like arrangement.

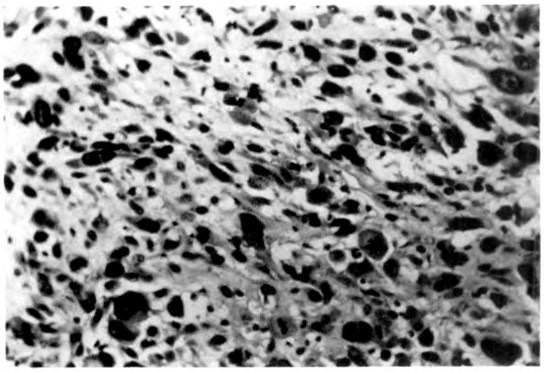

FIG. 8. Undifferentiated giant cell tumor, possibly a pleomorphic rhabdomyosarcoma (170×). This is a cellular tumor composed of rather loosely knit cells of different sizes and shapes. Giant forms are fairly common. Mitotic figures are noted in most high-power fields. There are some suggested ribbon cells, but this feature is not striking. No cross-striations are identified. The diagnosis is undifferentiated giant cell tumor. Pleomorphic rhabdomyosarcoma is a consideration.

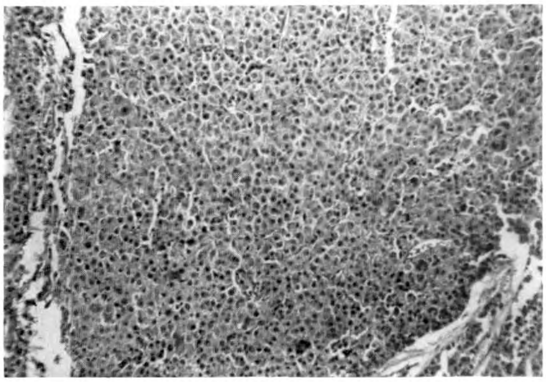

FIG. 9. Interstitial cell tumor, possibly a gynandroblastoma (73×). This tumor is composed of massive collections of moderately eosinophilic tumor cells. There is a generous amount of pale, eosin-staining cytoplasm, and there are oval nuclei which resemble one another, except for an occasional distorted or larger nucleus. It is difficult to find a single mitotic figure. This particular lesion was considered an interstitial cell tumor by several pathologists, although one felt that these cells were not truly Leydig cells. This pathologist was of the opinion that the lesion should be classified as a gynandroblastoma.

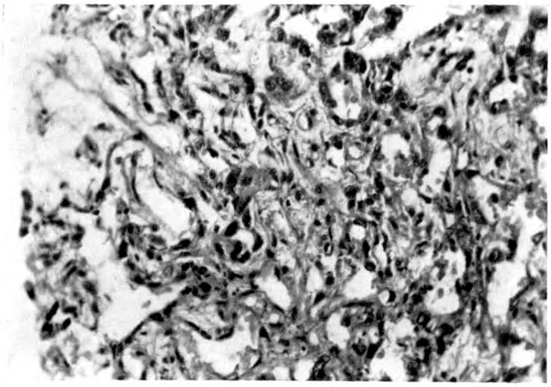

FIG. 10. Malignant mesothelioma with nephroblastoma elements (170×). This tumor has a rather loose stroma with poorly outlined cellular foci which are edematous and contain questionable pseudomucinous material. Here and there small distorted tubular formations are identified. Note the ragged appearance of the elongated cells, which led the pathologist to use the term mesothelioma.

symptoms and signs of widespread disease (hemoptysis, bone pain, neurologic symptoms, etc.) in 12 patients. In some patients epididymitis, hydrocele or spermatocele were among the diagnostic considerations mentioned. In 4 cases the testicular tumor was discovered incidentally on routine physical examination. In 1 case an abdominal mass was the initial sign and the diagnosis was made on biopsy at the time of the exploratory laparotomy. Subsequent exploration of the scrotum revealed the primary lesion which was too small to be detected on clinical examination.

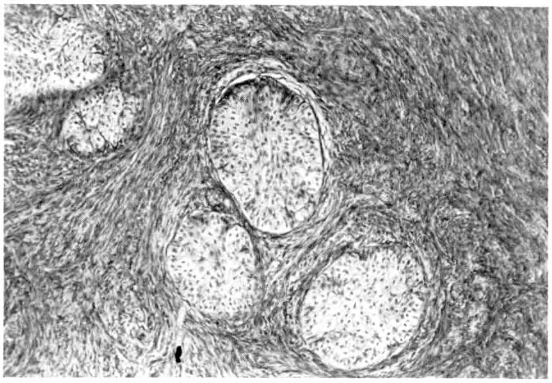

FIG. 11. Brenner tumor (73×). We have been unable to find a similar tumor of the testicle reported in our source material. Note the dense fibrous stroma. The cells which are in aggregates have the appearance of the cells noted in Walthard cell rests of the ovary.

The average duration of symptoms as recorded in 95 cases was found to be 2 months in choriocarcinomas, 5 months in embryonal carcinomas, 8 months in seminomas and 9 months in the teratomas.

Bilateral testicular tumors were diagnosed in 3 patients; the same histologic type (seminoma) was found in 2 cases, in 1 at 4 year and in the other at 9 year intervals. The third patient developed a seminoma on one side and 13 years later an embryonal carcinoma on the other.

Six tumors occurred in ectopic testes with 3 being seminomas, 2 teratomas and 1 embryonal carcinoma.

Gynecomastia was recorded in 2 patients, 1 with an embryonal carcinoma, the other with a teratoma.

TREATMENT

The intial therapy consisted of orchiectomy either alone or followed by roentgen therapy. In 2 patients with embryonal carcinoma, retroperitoneal lymph node dissection was carried out, but in both instances the retroperitoneal lymph nodes were microscopically free of tumor.

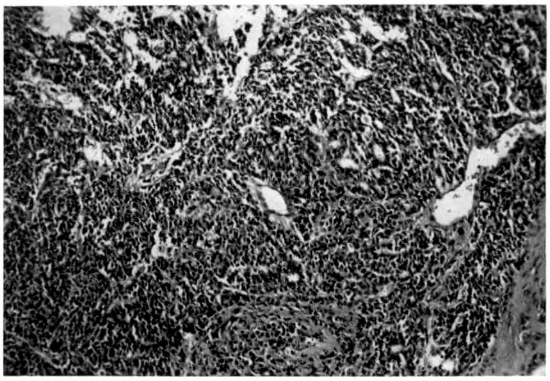

FIG. 12. Undifferentiated tumor (granulosa cell tumor suggested) (73×). This is a highly cellular moderately vascular tumor composed of small polyhedral and elongated cells with prominent nuclei. There is some tendency for these cells to form small acini, which might be considered Call-Exner bodies of granulosa cell carcinoma. The patient did not have any feminizing features.

Prior to 1958 the patients were treated with 250 kilovolt roentgen rays, employing a half value layer of 2.4 mm. of copper to the periaortic and mediastinal lymph nodes and of 1.1 mm. of copper to the inguinal and left supraclavicular areas. The abdomen and mediastinum were treated through anterior and posterior opposing fields, commonly measuring 15×20 cm. and 10×15 cm., respectively, and the inguinal-iliac and left supraclavicular areas through 10×10 cm. single anterior fields. Each field usually received 200 r/air per day. During the early years the tumor dose was not recorded but could be estimated and rarely exceeded 1,000 r over 10 to 12 days. This dose might, on occasions, be somewhat increased if lymph node metastases were clinically demonstrable. This tumor dose was maintained relatively constant regardless of the tumor type.

Since 1958 a 1,000 kilovolt roentgen-ray machine with a half value layer of 9 mm. of copper has been employed. The periaortic lymph nodes were treated through opposing anterior and posterior fields measuring about 8–10×20–30 cm. with the posterior field extending lower to oppose an anterior iliac and inguinal field. The tumor dose for seminomas varied between 2,000 and 2,600 r over 3 to 4 weeks but was increased to 4,000 r if large palpable abdominal masses were present. For the more radioresistant embryonal and teratomatous tumors, a dose between 3,000 and 4,000 r over 4 to 6 weeks was commonly delivered.

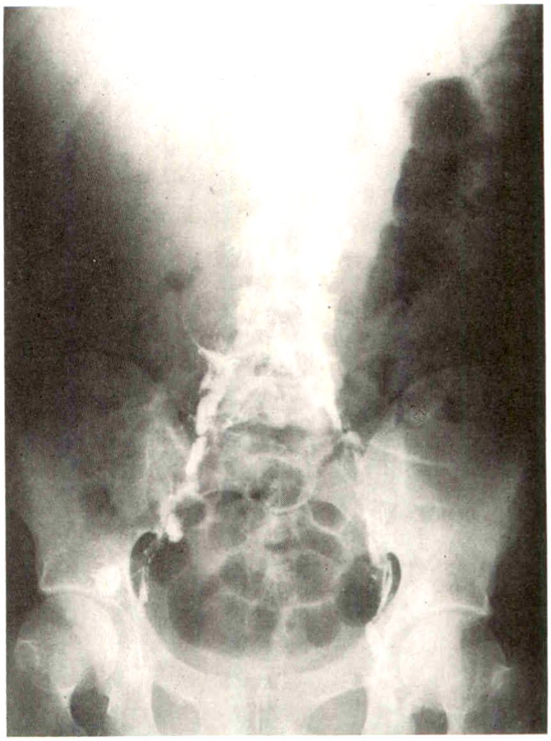

Fig. 14. Lymphogram of a patient having a mixed embryonal cell carcinoma and seminoma. Postinjection roentgenogram shows the contrast material in the lymphatic system. There is readily noted an obstruction to flow involving the pericaval lymph nodes just lateral to L4. The large metastatic deposit of tumor is outlined well by the contrast material. There is no filling of the pericaval lymph nodes superior to this lesion. The periaortic lymph nodes are normal. The haziness in the right upper quadrant is due to an enlarged liver, which clinically was thought due to metastases.

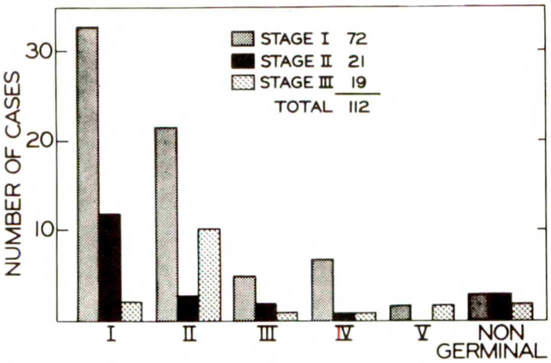

Fig. 13. Pathological grouping and clinical staging in 112 cases of testicular tumors.

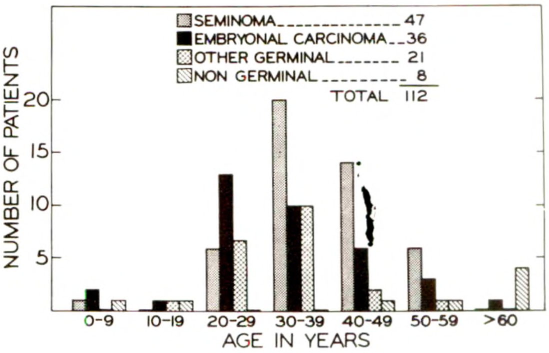

Fig. 15. Age distribution in 112 cases of testicular tumors.

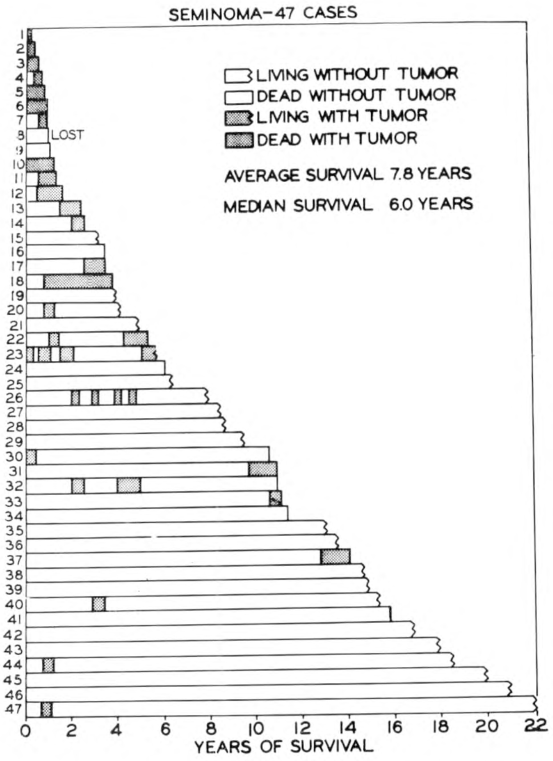

Fig. 16. Survival of 47 cases of seminoma from time of treatment.

The mediastinal and left supraclavicular lymph nodes were treated only if they were clinically or radiographically involved or if metastatic lymph nodes were found in the adjacent retroperitoneal area.

RESULTS

The survival periods for patients with different tumor types are given in Figures 16, 17, 18, and 19. As would be expected, the best 5 year survival rate was obtained in patients with seminoma (Group I) (Table I). An absolute 5 year survival rate of 63 per cent was recorded for the entire group, 68 per cent for Stage I and 56 per cent for Stage II cases. There were 2 deaths from intercurrent disease. One patient died from agranulocytosis a short time after roentgen-ray therapy and had no signs of residual or recurrent tumor. The second patient lived 15 years without recurrence and died of pneumonia.

There were 5 patients with metastases to regional lymph nodes who remained well for 5 years or longer. Two of these had large abdominal masses which regressed completely after radiation therapy, one being alive and well for 8 years and the other having recently received irradiation for recurrent left supraclavicular lymph node metastases.

There are 21 patients still living and all are free of tumor. The average survival in the whole group is presently 7.8 years, median survival 5.8 years. Three patients remained well from 9 to 12 years, but died from metastases. One exceptional patient who had a Stage III seminoma survived over 10 years and died of coronary thrombosis.

The 5 year survival rate was lower among patients with the more radioresistant embryonal carcinomas (Group II) and only 6 patients, all with Stage I tumors, survived. The absolute 5 year survival in Stage I was 32 per cent. Two patients died from intercurrent disease before the end of the 5 year period without evidence of recurrent

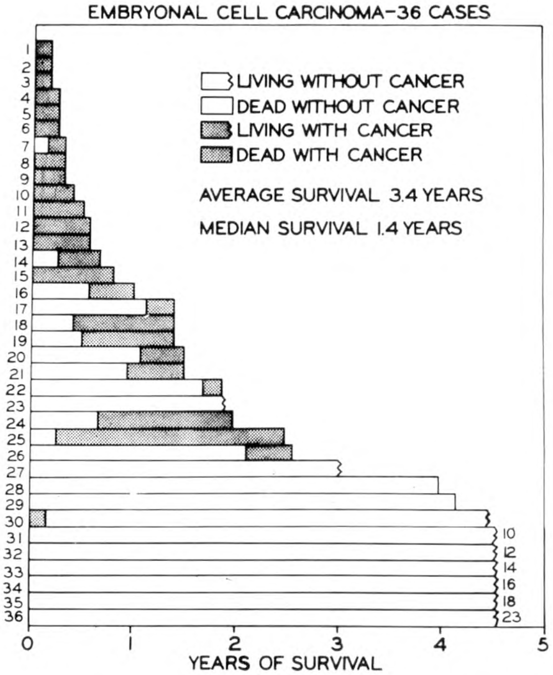

Fig. 17. Survival of 36 patients with embryonal carcinoma from time of treatment.

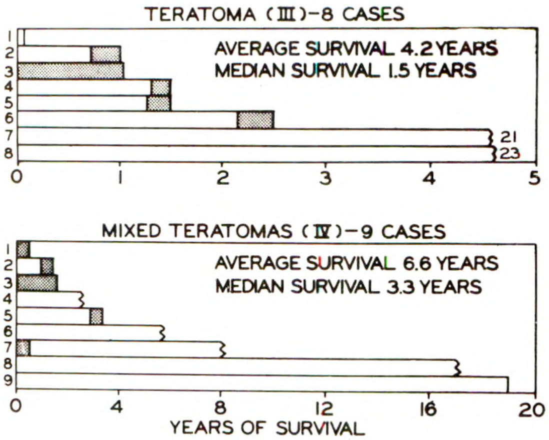

Fig. 18. Survival of 17 patients with teratoma from time of treatment.

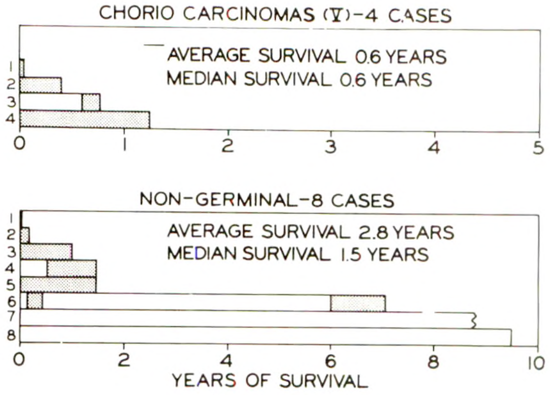

Fig. 19. Survival of 4 patients with choriocarcinoma and 8 patients with nongerminal testicular tumors from time of treatment.

testicular tumor, one from myelogenous leukemia, the other from a cerebrovascular accident. The average survival in this group is presently 3.4 years with 8 patients still alive. The median survival is 1.4 years.

There were 6 of 14 patients with teratomatous tumors surviving at least 5 years. It is of interest to note that the results appeared better in Group IV than in Group III, thus confirming the impression of Dixon and Moore[18] that coexistence of teratoma with either embryonal carcinoma or choriocarcinoma, or both, reduces the extremely malignant character of these tumors. One patient with Stage II, Group

Table I

TESTICULAR TUMORS

FIVE YEAR SURVIVALS ACCORDING TO CLINICAL STAGE

		Stage I	II	III	Total
Seminoma	Group I	21/31* = 68%	5/9 = 56%	1/3	27/43 = 63%
Embryonal carcinoma	Group II	6/19 = 32%	0/3	0/6	6/28 = 21%
Teratoma	Group III	1/5	1/2	0/1	2/8 = 25%
Teratoma	Group IV	4/6	—	—	4/6
Choriocarcinoma	Group V	0/2	—	0/2	0/4
Total germinal tumors		32/63 = 51%	6/14 = 43%	1/12 = 8%	39/89 = 44%
Nongerminal tumors		2/3	1/2	0/2	3/7

TEN YEAR SURVIVALS

		Stage I	II	III	Total
Seminoma	Group I	13/23 = 57%	3/6 = 50%	1/3	[illegible]/32 = 53%
Embryonal carcinoma	Group II	5/12 = 42%	0/1	0/2	5/15 = 33%
Teratoma	Group III	1/5	1/2	0/1	2/8 = 25%
Teratoma	Group IV	2/2	—	—	2/2
Choriocarcinoma	Group V	—	—	0/2	0/2
Total germinal tumors		21/42 = 50%	4/9 = 44%	1/8	26/59 = 44%

* Number surviving/number treated.

Table II

TESTICULAR TUMORS
FIVE YEAR SURVIVALS ACCORDING TO INITIAL THERAPY

		Surgery Alone			Surgery and Irradiation			Total
		Stage I	II	III	Stage I	II	III	
Seminoma	Group I	3/7* 43%	0/1	—	18/24 75%	5/8 62%	1/3	27/43 63%
Embryonal carcinoma	Group II	0/5	—	0/2	6/14 43%	0/3	0/4	6/28 21%
Teratoma	Group III	1/1	—	—	0/4	1/2	0/1	2/8
Teratoma	Group IV	—	—	—	3/5	1/1	—	4/6
Choriocarcinoma	Group V	0/1	—	0/2	0/1	—	—	0/4
Total germinal tumors		4/14 29%	0/1	0/4	27/49 55%	7/14 50%	1/8	39/89 44%
Nongerminal tumors		2/2	—	0/1	0/1	1/2	0/1	3/7

* Number surviving/number treated.

III teratoma died from agranulocytosis shortly after radiation therapy to the abdomen and mediastinum.

The average survival in Group III is 4.2 years with 2 patients still alive, and in Group IV, 6.6 years with 4 patients still living.

The choriocarcinomas proved fatal regardless of stage and the average survival was only 0.6 years.

The nongerminal tumors included a variety of histologic types. There were 3 five year survivors; 2 of these were classified as Stage I (one malignant mesothelioma and the other a Brenner tumor) and the third as Stage II (a fibrosarcoma with inguinal lymph node metastases). This patient developed metastases 6 years after therapy and died.

The 10 year survival in the group of 59 patients treated before 1953 was 44 per cent, with 50 per cent Stage I and 44 per cent Stage II cases surviving. The best 10 year survival was again in the group of 32 patients with seminoma (53 per cent) as compared to 5 of 15 patients with embryonal carcinoma and 4 of 10 patients with teratoma (Table I).

In order to evaluate the influence of radiation therapy on the length of survival, the patients were divided into two groups, the first consisting of those who had no radiation therapy immediately following the orchiectomy and the second of those who did have postoperative radiation therapy (Table II).

In spite of the limited number of patients in each group, the difference in the survival figures was quite striking. Thus, among the Stage I seminomas 3 of the 7 patients (43 per cent) treated with orchiectomy alone as compared with 18 of 24 patients (75 per cent), treated with orchiectomy and postoperative roentgen-ray therapy, survived 5 years. In Stage II, 5 of 8 patients with seminoma survived 5 years after orchiectomy and postoperative roentgen-ray therapy. One patient underwent orchiectomy, but received no postoperative radiation therapy in spite of the presence of palpable abdominal masses. When admitted for the first time to the University Hospitals 7 months later, he had extensive abdominal and pulmonary metastases and expired a few months later.

In Stage I embryonal carcinoma (Group

II), the effect of postoperative radiation therapy was also apparent with 6 of 14 patients surviving 5 years or longer. There was no survivor among 5 patients treated with orchiectomy alone. Two patients underwent retroperitoneal lymph node dissection. The lymph nodes were reported negative for tumor on microscopic examination; nevertheless, both patients died from distant metastases within 2 years. There were no 5 year survivors among patients with Stage II or III embryonal carcinomas.

Among the 8 patients with teratomas with or without seminoma (Group III), only 2 patients survived the 5 year period. One patient was admitted with a hard 9 cm. testicular mass. Because of tumor nodules present on the scrotal skin, the patient was recorded as a Stage II case, was given radiation therapy both before and after the orchiectomy and was found to be living free of recurrence 23 years later. The second patient had a Stage I teratoma and lived free of recurrence 21 years after orchiectomy alone.

All 6 patients with mixed teratomas (Group IV) treated before 1959 received postoperative roentgen-ray therapy and 4 survived 5 years or more.

Finally, the influence of the radiation dose on the 3 year survival rate was analyzed (Table III). The study had to be limited to the 3 year period because the increased dosages using higher energy radiation were not introduced until 1958 and the number of patients was therefore limited. Nevertheless, the results so far support the opinion that improved survival can be obtained with the higher dosage. In Stage I seminoma 82 per cent of the patients survived even after less than 1,000 r, illustrating the marked radiosensitivity of this tumor. The 4 patients who received doses in excess of 1,000 r (ranging from 1,400 to 2,600 r to the retroperitoneal

Table III

TESTICULAR TUMORS

THREE YEAR SURVIVALS ACCORDING TO DOSE OF RADIATION

	Stage I Dose r/tumor		Stage II Dose r/tumor		Stage III Dose r/tumor		Total
	<1,000	>1,400	<1,200	>1,500	<1,000	>1,200	
Group I Seminoma	19/22* 86%	4/4 100%	3/6 50%	2/3 67%	0/2	1/1	29/38 76%
Group II Embryonal carcinoma	4/11 36%	3/4 75%		0/3	0/1	0/3	7/22 32%
Group III Teratoma	0/4	—	1/1	0/1	—	0/1	1/7
Group IV Teratoma	2/3	2/2	1/1	—	—	—	5/6
Group V Choriocarcinoma	—	—	—	—	0/1	—	0/1
Total	25/40 63%	9/10 90%	5/8 63%	2/7	0/4	1/5	42/74 57%

* Number surviving/number treated.

lymph nodes) are all well. The higher dosage assumes increased importance in Stage II tumors and in the more radioresistant embryonal carcinomas.

DISCUSSION

INCIDENCE

For the 20 year period studied, the total cancer deaths among males in Wisconsin averaged about 2,900 per year, while the mean annual death rate for malignant neoplasms of the testis amounted to 19.5.[81] This represents an incidence of 0.67 per cent of all fatal malignancies in males, a figure not significantly different from the 0.64 per cent reported by Gilbert and Hamilton[27] and Dixon and Moore[19] for the entire United States, but somewhat higher than the 0.52 per cent reported from England and Wales[68] and the 0.3 per cent reported from Norway.[59]

Statistics on admissions at the University of Wisconsin Hospitals, available only for the 12 year period between 1949 and 1960, indicated a total of 162,456 admissions. During that same period there were 68 patients admitted with malignant testicular tumors, an incidence of approximately 0.042 per cent. This may be compared with the incidence of 0.078 per cent from 9 different hospitals reported by Campbell;[8] of 0.063 per cent of all male admissions at the University of Iowa reported by Culp[13] and of 0.015 per cent of all admissions at the Veterans Hospital, Bronx, New York.[39] It is therefore readily apparent that testicular tumors are relatively infrequent and most institutions require long periods of time in order to accumulate significant numbers. A notable exception occurred during the last World War at the hospitals serving military personnel; a high incidence of testicular tumors among the Armed Forces, from 3 to 10 in 100,000[18,44,50,58] was reported. A number of studies analyzing this unique material has appeared[19,22,23,24,25,42,43,44,49,50,58,63,64] and has greatly influenced later studies in other institutions. Such a high incidence among military personnel can be explained on the basis of the characteristic age distribution of germinal testicular tumors with the peak incidence occurring in young adults between 20 and 40 years of age.[13,17,18,19,29,33,36,39,44,48,57,63,64,65,67,71,72,75] In the age groups from 20 to 35 years, testicular tumors consitute one of the most common forms of malignancy in the male.[63]

In the present series the peak incidence of the seminomas occurred between 30 and 39, of the embryonal carcinomas between 20 and 29 and of the other germinal tumors between 30 and 39 years of age—a finding in general accord with reports by others.[25,36,39,57,58,63,64,72,79]

ECTOPY

The incidence of coexisting cryptorchism and testicular neoplasia was 5.4 per cent (6 of 112) in our material, which is within the range of that observed by others who have reported from 4.8 per cent to 30 per cent of all testicular tumors occurring in undescended testes,[17,27,28,29,40,47,48,50,55,56,67,69] but higher than the 2.4 per cent reported among military personnel.[18] The increased incidence of neoplasia in cryptorchid testes is well established.[8,13,15,17,27,33,40,44,50,56,59,72,79] According to different estimates, malignant tumors occur from 20 to 220 times more frequently in undescended testes than in the normally descended organ,[17,44,48,69] but the validity of some of these statistical data has been questioned.[9,30] In some patients with unilateral cryptorchism, tumors have developed in the normally descended, rather than the ectopic, testis. Gilbert and Hamilton[27] reported 23 such patients; Rusche[71] collected 4 and Moffat[54] observed 2. These findings suggest that ectopy *per se* is not the essential carcinogenic factor, but may be only one of the many manifestations of developmental disturbances (perhaps mediated by hormones), which under certain circumstances also can lead to tumor induction. Orchiopexy has not prevented the development of testicular tumors in a number of patients.[26,27,48,63,71] It is also well established that patients with bilateral scrotal testes, successfully treated for a tumor in one testis, exhibit an increased incidence of tumor development in the other testis. The incidence among such patients has been estimated to be 0.7 per cent, as compared to 0.0013 per cent in the general population previously not afflicted with this disease.[26,27,32] A much higher incidence was found among patients with bilateral ectopy and previously treated testicular malignancy with 24.6 per cent developing a tumor in the opposite testis.[26]

In the present series, there were 3 patients with bilateral testicular tumors, an incidence of 2.7 per cent.

The results of treatment of cryptorchids who have had orchiopexy and later developed testicular neoplasms have been very poor.[26,40] On the other hand, the survival of patients with testicular tumors developing in previously untreated ectopic testes has been quite satisfactory.[18,28,48] The results in the present series seem to confirm this impression: among the 6 cryptorchids, there were 4 with Stage I tumors (3 seminomas and 1 embryonal carcinoma), 3 of whom were free of disease 3, 11 and 22 years respectively after treatment. The fourth patient was lost. The fifth patient had a Stage II teratoma (Group IV) and survived without recurrence for 8 years. The sixth patient had a Stage II embryonal carcinoma and died 4 months after treatment.

HORMONAL INFLUENCES

Gynecomastia was encountered in 2 patients only. Assays for chorionic gonadotrophins and follicle stimulating hormones were not performed consistently. Such assays were found to be unreliable by Lewis,[50] who reported positive findings in 35 per cent of control patients without testicular tumors. Rapidly increasing hormone titer occurring after orchiectomy on patients with or without gynecomastia signifies extensive tumor metastases containing trophoblastic elements and is therefore an ominous sign.[7,18,25,29,56,57,63,71,72] Hyperplasia of interstitial cells associated with testicular tumors has been found to be an unfavorable prognostic sign and so has presence of hemorrhagic necrosis and vascular invasion by tumor.[18]

ANALOGOUS TESTICULAR AND OVARIAN TUMORS

All of the germinal tumors of the testis have counterparts in the ovary.[18,19] Thus, the seminomas of the testis correspond closely to the dysgerminomas of the ovary.[75,76] Embryonal carcinomas, teratomas and choriocarcinomas occur in both testis and ovary, but the relative frequency varies,[18] and the ovarian tumors commonly attain a higher degree of differentiation. No counterparts of ovarian cystadenocarcinomas have been found in the testis; however, examples of a granulosa cell and a Brenner tumor of the testis were encountered in the present material.

COMMENTS ON THERAPY

There is overwhelming evidence to indicate that radiation therapy aids in the control of metastases and, therefore, improves the results of treatment of testicular tumors. In a compilation of statistics, the 3 to 5 year survival figures varied from 5 per cent to 49 per cent, with an average of 15 per cent in 1,182 patients treated with orchiectomy alone, as compared to a range of 23 per cent to 88 per cent with an average of 45 per cent in 1,133 patients treated with orchiectomy and radiation therapy (Table IV).

SEMINOMAS

The remarkable radiosensitivity of the seminomas is now generally recognized.[3,6] Thus orchiectomy and radiation therapy yielded 5 year survival figures varying from 45 per cent to 94 per cent with an average of 65 per cent in 1,215 cases of seminoma collected from different institutions (Table V). In a more recent series collected from data published between 1950 and 1960, the 5 year survival rates ranged from 45 per cent to 94 per cent with an average of 73 per cent in 1,088 cases, some of which had undergone retroperitoneal lymph node dissection (Table VI). Included in the latter

TABLE IV

TESTICULAR TUMORS
THREE TO FIVE YEAR SURVIVALS
AFTER ORCHIECTOMY WITH AND WITHOUT POSTOPERATIVE RADIATION THERAPY

	Without		With	
	No.	%	No.	%
Kober, 1899, cited in Reference 29	23/114*	20[x]		
Chevassu, 1906, cited in Reference 29	13/114	11[x]		
Tanner,[74] 1922	25/465	5[xx]		
Rea,[69] 1931	34/257	13[xx]		
Rea,[69] 1931	5/38	13[xx]		
Grevillius,[29] 1937	41/83	49[xx]	25/52	48[xx]
Leddy and Desjardins,[47] 1938	2/5	40	47/161	29
Payne,[66] 1938	15/32	47[xxx]		
Cabot and Berkson,[5] 1939	15/31	48	39/74	53
Higgins and Buchert,[33] 1939	5/24	21	11/31	35
Nesbit and Lynn,[56] 1946	5/19	26[xx]	14/61	23[xx]
Pendergrass *et al.*,[65] 1946			18/41	44
Gordon-Taylor and Wyndham,[28] 1947			178/396	45
Leucutia *et al.*,[48] 1948			45/81	56
Prossor,[67] 1950			42/90	47
Paterson,[62] 1952			53/105	50
Kunkler *et al.*,[45] 1952			36/41	88
Total	183/1,182=15%		508/1,133=45%	

* Number surviving/number treated.

No asterisk indicates 5 year survivals; x=3 year survivals; xx=4 year survivals; xxx=4 of the 15 survivors had received radiation therapy.

group, however, are the figures published by Dixon and Moore[18,19] computed by the life table method and by subtracting the number of patients dead of tumor from the total number of cases treated, exluding the number of cases lost to follow-up or dead of intercurrent disease and also excluding all the inoperable (clinical Stage II and III) cases. Therefore, these data are not directly comparable.

In seminomas *without* clinical signs of metastases, the 5 year survival rates varied between 59 per cent and 89 per cent with an average of 80 per cent in 594 cases collected from the literature (Table VII).

In seminomas *with* clinical evidence of metastases, the 5 year survival rates ranged from 18 per cent to 61 per cent averaging 29 per cent in 210 cases (Table VII).

These tumors are curable with radiation therapy even in the advanced stages after metastases have occurred to retroperitoneal, mediastinal or left supraclavicular lymph nodes, and are demonstrable clinically.[22,79]

The great majority of the patients in the present series was treated before 1958 with small doses of orthovoltage roentgen-ray therapy. Nevertheless, in patients with seminoma, the 5 year survival was considerably increased with the added irradiation, thus illustrating the pronounced radiosensitivity of these tumors.

There is reason to believe, however, that further improvement in the results can be achieved by increased dosage,[36] which, when properly fractionated, can be most conveniently delivered with high energy equipment.[21] Some seminomas contain foci of more radioresistant cells[25] sometimes undetected by routine sectioning of the primary tumor. Thus, Dixon and Moore[18] reported that in 14 per cent of their seminoma cases trophoblastic cells were present, and in 23 patients with seminoma, postmortem examination revealed metastasis containing embryonal carcinoma in 6, choriocarcinoma in 2, and teratoma in 1.

Therefore, even though the majority of the seminomas in the Stage 1 category can be controlled with radiation dosages of 2,000 r delivered over 2 weeks,[22,72] some authors[17,22,36] have obtained better results with higher dosages (2,700–3,000 r over 3 weeks). Larger metastatic deposits may also require higher dosage because of poor vascularization and hypoxia.

In patients with seminoma, without clinically demonstrable metastases, 5 year cure rates of 90 per cent should be within the realm of possibility with simple orchiectomy and adequate radiation therapy to the regional lymph nodes.[21,63]

Distant metastases from seminoma also respond well to irradiation and prolonged palliation can be obtained. As an example, 1 patient in our series, who had solitary pulmonary and multiple cervical and inguinal lymph node metastases, received roentgen-ray therapy and survived for 10 years without evidence of recurrence. There

Table V

TESTICULAR TUMORS
FIVE YEAR SURVIVALS
AFTER ORCHIECTOMY OR RETROPERITONEAL LYMPH NODE DISSECTION AND POSTOPERATIVE RADIATION THERAPY

	Simple Orchiectomy and Radiation Therapy				Retroperitoneal Lymph Node Dissection and Radiation Therapy			
	Seminoma		Others		Seminoma		Others	
	No.	%	No.	%	No.	%	No.	%
Grevillius[29], 1937	23/39	59*	2/13	15*				
Cabot and Berkson,[6] 1939	32/45	71	7/29	24				
Ahlbom,[1] 1947	42/65	65	17/54	31				
Kelby and Stenstrom,[41] 1947	9/16	56	9/56	16				
Sauer *et al.*,[72] 1948	39/68	57	31/75	41				
O'Connell and Geschickter,[58] 1950	45/75	60	26/142	18				
Boden and Gibb,[4] 1951	54/96	56	9/32	28				
Dean,[17] 1951	63/135	47	56/229	24				
Kaplan *et al.*,[39] 1951	15/33	45	20/75	27				
Dixon and Moore,[19]† 1952					282/315	90	241/517	47
Rusche,[71] 1952	26/38	68	41/77	53				
Kimbrough and Cook,[44] 1953					116/203=57%			
Cox,[13] 1954	48/68	71	11/32	34				
Moffat,[54] 1954	15/16	94	2/6	33				
Friedman,[21] 1956	78/94	83						
Notter,[57] 1956	76/107	71	36/107	34				
Whittle,[79] 1957	48/62	77	24/37	65				
Staubitz *et al.*,[73] 1958	14/22	64	3/19	16			27/39	69
Höst and Stokke,[36] 1959	115/156	74	60/144	42				
Patton and Mallis,[64] 1959	20/36	56	11/91	12	83/100	83	89/143	62
Parker and Holyoke,[61] 1960	32/44	73	21/38	55				
Total	794/1,215	65	386/1,256	31	365/415	88	357/699	51

* 4 year survivals.

† Only operable cases, relative 5 year survivals.

Table VI

TESTICULAR TUMORS

FIVE YEAR SURVIVALS ACCORDING TO DIFFERENT GROUPS

	Group I		II		III		IV		V		Miscellaneous		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
O'Connell and Geschickter,[68] 1950	45/75	60	10/75	13	16/67=24%				—		—		71/217	33
Dean,[17] 1951	63/135	47	23/110	21	4/13=31%				0/11	0	29/95	31	119/364	33
Kaplan *et al.*,[39] 1951	15/33	45	15/51	29	4/15=27%				1/9	11	—		35/108	32
Rusche,[71] 1952	26/38	68	27/38	71	10/18	56	4/18	22	0/3	0	—		67/115	58
Dixon and Moore,[19]* 1952	282/315	90	59/165	36	52/73	71	130/273	48	0/6	0	—		523/832	63
Moffat,[54] 1954	15/16	94	1/2	50	1/4=25%								17/22	77
Notter,[57] 1956	76/107	71	6/39	15	5/8	63	24/59	41	—		1/1		112/214	52
Staubitz *et al.*,[73] 1958	14/22	64	7/18	39	8/17=47%				0/2	0			29/59	49
Höst and Stokke,[36] 1959	115/156	74	23/59	39	19/39=49%						18/46	39	175/300	58
Patton and Mallis,[64] 1959	111/147	76	58/139	42	42/120=39%						11/15	73	222/421	54
Parker and Holyoke,[61] 1960	32/44	73	7/20	35	14/18=78%								53/82	65
Friedman and Di Rienzo,[23] 1963			25/83	30									25/83	30
Friedman and Di Rienzo,[24] 1963			15/54	28									15/54	28
Total	794/1,088=73		276/853=32		333/742=45%				1/31=3		59/157=38		1,463/2,871=51	

* Dixon and Moore included only operable cases. The survival figures were obtained by subtracting the number of cases dying of tumor from the total number of cases treated. The number of cases lost or dead of intercurrent disease is unknown.

are several reports of similar cases in the literature.[22,53,60,80]

EMBRYONAL AND TERATOID TUMORS

The embryonal carcinomas and the teratomas are generally more radioresistant, even though some variation in radiosensitivity has been observed.[1,24,60,67] Ahlbom[1] encountered some tumors with embryonal carcinomatous and mixed teratomatous elements that possessed a radiosensitivity which approached that of the seminomas, while others were only moderately radiosensitive. Friedman[21] observed that for immature cartilage in teratoid tumors the lethal dose was 2,400 r, but for some mature glandular structures it exceeded 5,000 r. Tumor doses of 4,000 to 5,000 r delivered over 4 to 6 weeks have, therefore, been recommended.[17,21]

Such high doses may approach or even exceed the tolerance of certain vital normal tissues[45,62] and great caution must be exercised so as to avoid irreparable damage to the gastrointestinal tract and the kidneys.[16,21,23,24,45,50,62]

No such complications were encountered in the present series as the dose was low, although in a few patients 4,000 r of 1,000 kilovolt roentgen rays to the retroperitoneal lymph node areas were readily tolerated, provided the weekly dosage did not exceed 800 to 1,000 r to fields sufficiently limited so as to avoid the kidneys.

Irradiation of excessively large fields may lead to serious bone marrow depression. Two such cases treated with orthovoltage roentgen rays were encountered: (1) A 50 year old man with a Stage I seminoma received from 1,000 to 1,600 r estimated central axis midplane dose over 11 days to large fields covering the inguinal, iliac, periaortic, mediastinal and left supraclavicular areas. He died 1 year later from agranulocytosis, and autopsy revealed severe myelofibrosis. (2) A 28 year old patient with Stage II teratoma received 2,000 r calculated central axis midplane dose to a 15×20 cm. field to the abdomen and 1,500 r to a 10×15 cm. field to the mediastinum over a period of 20 days. A white blood cell count 2 weeks later was reported as 800/mm.^{3}, and the patient died with all signs of bone marrow depletion 2½ weeks after completion of irradiation.

Satisfactory results have been reported without prophylactic irradiation of the mediastinum and the left supraclavicular regions in Stage I tumors.[1] Such prophylactic irradiation is still recommended in Stage II tumors because of the high incidence of subsequent metastases to lymph nodes in these areas.[38]

The prognostic importance of clinical staging of testicular tumors was emphasized by Whittle[79] and was clearly apparent in our present material. The superior results obtained in the earlier stages again call attention to the importance of an early diagnosis. Every mass in the scrotum must be considered malignant until proven otherwise,[16,25] and there can be no substitute for an immediate orchiectomy, which is so essential for a correct histologic diagnosis and planning of further therapy in testicular tumors.[16]

It is generally agreed that preoperative irradiation to the primary tumor should be avoided, since it distorts the histologic architecture and makes identification difficult or impossible.[71,72] There is no evidence to suggest that preoperative irradiation increases the survival beyond that which can be obtained with postoperative radiation therapy to the retroperitoneal and inguinal lymph nodes.[65]

The radioresistance of the embryonal and teratoid tumors is illustrated by the lower 5 year survival rates obtained with simple orchiectomy and postoperative radiation therapy as compared with those obtained in seminomas. Thus, in a compilation of statistics from the literature, the 5 year survival figures varied between 12 per cent and 65 per cent, averaging 31 per cent for 1,256 patients (Table V). This is less

Table VII

TESTICULAR TUMORS
FIVE YEAR SURVIVALS IN CASES WITH AND WITHOUT METASTASES

	Seminomas				Embryonal and Teratoid Tumors			
	Without		With		Without		With	
	No.	%	No.	%	No.	%	No.	%
Cabot and Berkson,[5] 1939	36/49	73	6/15	40	10/27	37	2/14	14
Ahlbom,[1] 1947	35/42	83	7/23	30	17/29	59	0/25	0
Prossor,[67] 1950	32/48	67			5/9	56		
Boden and Gibb,[4] 1951	40/50	80	14/46	30	5/10	50	1/7	14
Kaplan *et al.*,[39] 1951	13/22	59	2/11	18	15/34	44		
Cox,[12] 1954	44/56	79			8/22	36		
Friedman,[21] 1956	68/76	89						
Notter,[57] 1956	70/80	88	5/27	19	30/60	50	5/24	21
Whittle,[79] 1957	34/39	87	14/23	61*	23/32	72	1/5	20*
Höst and Stokke,[38] 1959	106/132	80	12/65	18	40/71	56		
Friedman and Di Rienzo,[23] 1963					25/48	52	0/35	0
Friedman and Di Rienzo,[24] 1963					15/34	44	0/20	0
Total	478/594	80	60/210	29	193/376	51	9/130	7

* Stage II only.

than half the corresponding average 5 year survival of 65 per cent reported for 1,215 cases of seminoma by the same authors.

The 5 year survival rates in patients with embryonal and teratoid tumors without clinical signs of metastases varied between 36 per cent and 72 per cent, averaging 51 per cent in 376 patients (Table VII). The extremely unfavorable prognosis in patients with clinically evident metastases from such tumors is illustrated by the figures in this collected series where only 9 patients of a total of 130 patients treated (7 per cent) survived 5 years (Table VII).

The 5 year survival rates in the collected series of patients with embryonal carcinoma (Group II) were below those observed in patients with teratomas (Group III and IV), varying between 13 per cent and 71 per cent, averaging 32 per cent for 853 patients with embryonal carcinoma, as compared to an average of 45 per cent for 742 patients with teratomas (Table VI). The prognosis in Group III teratomas (with or without seminomatous elements) was considerably better (5 year survival rates varying between 56 per cent and 71 per cent) than in Group IV teratomas (with embryonal or choriocarcinomatous elements, with or without seminoma) (5 year survival rates varying between 22 per cent and 48 per cent) (Table VI).

In our own material there were 12 patients with embryonal or teratoid carcinomas who lived without clinical evidence of recurrence for 5 years or longer (6 embryonal carcinomas and 5 teratomas, all Stage I, and I Stage II, Group III teratoma). The 6 patients with embryonal carcinoma are still alive and free of clinical signs of tumor from 10 to 23 years after simple orchiectomy and radiation therapy. Four of the patients with teratomas are alive and well from 5 to 23 years after treatment; the fifth patient died without recurrence 19 years after simple orchiectomy and irradiation. All these patients received low doses of radiation (5 in the range of 500 to 650 r, 3 about 1,000 r, one 1,500 r and one about 3,000 r to the retroperitoneal area at dose rates of 200 r/air a day to each of two opposing fields). One might have reason to question the contribution of radiation therapy in these cases and assume that the retroperitoneal lymph nodes might have been negative for metastases at the time of the orchiectomy.

In the other group, however, 5 of the 6 patients with the same types of tumor, all Stage I, treated with simple orchiectomy without irradiation, died of metastases after an average survival of only 17 months. The sixth patient is living without recurrence 21 years after the orchiectomy. In this group there were also 2 patients who underwent radical retroperitoneal lymph node dissection but died of metastases.

RETROPERITONEAL LYMPH NODE DISSECTION

The incidence of metastases to the retroperitoneal lymph nodes from testicular tumors has been found to be very high even in the clinical Stage I tumors: from 57 per cent to 62 per cent in embryonal carcinoma[23,24] and from 12.5 per cent to 32 per cent in seminoma.[22,50,78] The first metastatic emboli usually settle in the periaortic and pericaval lymph nodes extending from the aortic bifurcation to the level of the kidney pedicles,[2,7,11,12,20,29,32,44,47,48,51,78] after floating along lymph vessels which provide direct communication from the lymphatics of the testis.[37]

Occasionally, there is direct connection between the lymphatics of the testis and a lymph node in the external iliac chain at the pelvic brim immediately in front of the ureter.[37,51] If the tumor has extended into the epididymis, metastases occur with increased frequency in the external iliac lymph nodes.[51] The inguinal lymph nodes may become involved if the tumor has perforated the tunica vaginalis (which occurs only infrequently unless biopsy has been taken) or if extensive periaortic lymph node metastases have blocked the lymphatic drainage.[2,51]

It was the hope of many surgeons that a radical dissection of the entire chain of lymph nodes along the spermatic cord up to the level of the kidney pedicles would result in an increased cure rate.[73] The technical difficulties of completely removing metastatic lymph nodes were considerable, however. Frequently dense adhesions to the great vessels made the operation unsatisfactory,[17] and the exact role of the radical retroperitoneal lymph node dissection is still disputed.[17,28,46,49,50,53,61,64,73] Most authors agree that in the radiosensitive seminomas such operations are unnecessary.[49,61,63,64] In the more radioresistant tumors, however, the operation might aid in the eradication of residual lymph node metastases.

The early results published by Hinman[34] were not encouraging. He reported on 100 cases, and in 80 the radical retroperitoneal lymph node dissection had been successful. At the time of the report, 35 per cent had died of metastases, 64 per cent were still living, but only 17 had been alive and well for 5 years after the operation. For a while, the operation was abandoned, but during the last war great strides were made in reducing the operative mortality which had earlier been reported as high as 12 to 15 per cent.[33] Thus, no postoperative mortality was reported in subsequent series of patients by Lewis[50] (169 cases), Kimbrough and Cook[44] (93 cases), Dowd *et al.*[20] (32 cases), and Cahill[7] (29 cases). Therefore, in the hands of experienced surgeons, the operation now appears quite safe. Most surgeons recommend bilateral retroperitoneal lymph node dissection because of the frequent metastases to the opposite side,[2,11,20,46,52,63] but, nevertheless, do not rely entirely on the surgical dissection for the complete eradication of all the tumor. In most published series, therefore, postoperative radiation therapy has been employed. This is quite understandable when considering the rich network of anastomosing lymphatics surrounding the aorta and the inferior vena cava. Lymphangiography has revealed retroperitoneal lymph nodes with changes suggestive of metastatic involvement remaining even though a complete lymph node dissection was done.[77] Some authors have expressed concern about the possibility of dissemination of tumor cells during the surgical manipulations.[23,24] Claims for improved survival statistics following radical retroperitoneal lymph node dissection are sometimes difficult to evaluate because of the varying dosages and techniques of postoperative irradiation applied and the selection of the case material.[7,16,46.49,50,72,73]

Friedman and Di Rienzo[23] reported on 9 patients with embryonal carcinoma, clinical Stage I, treated with simple orchiectomy and radiation therapy. Eight of these survived at least 5 years. Retroperitoneal lymph node dissection followed by irradiation was performed in 39 patients. In 15 of them the lymph nodes were negative for tumor, but only 9 survived 5 years. In 24 patients the lymph nodes were positive for metastatic carcinoma and 8 of these survived 5 years or more. Therefore, the results seemed better with the simple orchiectomy and postoperative irradiation than with the radical lymph node dissection and postoperative radiation therapy. With clinically evident metastases, however, no survivor among 55 patients was reported.[23,24]

Dixon and Moore[18] compared the results of simple orchiectomy and irradiation with orchiectomy and radical retroperitoneal lymph node dissection followed by radiation therapy and computed the 2 year mortality rates from tumor as follows: in embryonal carcinoma, 63 per cent (125 cases) versus 44 per cent (32 cases); in Group III teratomas, 24 per cent (58 cases) versus 10 per cent (10 cases); and in Group IV teratomas, 50 per cent (217 cases) versus 43 per cent (49 cases). These figures, therefore, suggested a reduced death rate from recurrent tumor after the more radical operation. It was not stated, however, whether the two groups were comparable as to clinical stage and radiation dose. Staubitz *et al.*[78] reported that 27 of 39 patients (69 per cent) with embryonal and teratoid tumors were alive 5 years after radical retroperitoneal lymph node dissection and only 3 of 19 patients (16 per cent) after simple orchiectomy. Both groups had received postoperative radiation therapy (Table v). Similarly, Patton and Mallis[64] reported 89 of 143 cases (62 per cent) surviving 5 years after retroperitoneal lymph node dissection and only 11 of 91 cases (12 per cent) after simple orchiectomy (Table v). All patients had embryonal carcinoma or teratoma and received postoperative radiation therapy. Further support of the value of retroperitoneal lymph node dissection was provided by the same authors who reported that 19 of 40 patients with histologically proven retroperitoneal lymph node metastases from embryonal carcinoma or teratoma survived more than 5 years, and 16 were living and well from 5 to 13 years, without ever having received postoperative radiation therapy. There were 13 patients with embryonal carcinomas and 6 with teratomas among the survivors. Similar isolated cases have also been reported by others.[7,20,35]

If widespread metastases are present, chemotherapy may offer some benefit. Whitmore[78] recommended a combination of chlorambucil, methotrexate and actinomycin D for treatment of patients with disseminated testicular tumors. In a series of 38 patients, 5 were alive and without evidence of disease from 13 to 56 months after onset of therapy; 3 of them had received the triple chemotherapy, 1, alkylating agent and actinomycin D, and 1, antimetabolite only.

In the present series, 12 patients received chemotherapy for disseminated tumors. In 11 of them the average survival was 10.5 months, ranging from 3 to 19 months. The twelfth patient, who had embryonal carcinoma with pulmonary and retroperitoneal lymph node metastases, is alive 4½ years after initiation of therapy with metramycin and there has been complete regression of all demonstrable tumor. This patient received no radiation therapy.

The rapid progression of the choriocarcinomas has not, as a rule, been altered by presently known methods of therapy,[17,18,39,64,71,73] although isolated cases discovered early may have survived.[39]

SUMMARY

A series of 112 consecutive patients with histologically proven testicular tumors collected over a 20 year period has been analyzed and the principles of management are discussed.

The following factors were considered to be of importance: the histologic features, the anatomic extension (clinical stage) and the radiosensitivity of the tumor, the resectability of retroperitoneal radioresistant tumor metastases and the susceptibility of disseminated tumor to palliative chemotherapy.

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Patients in this series irradiated before 1958 were under the supervision of the late Dr. E. A. Pohle, Professor of Radiology.

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GRANULOMA INGUINALE WITH BONE INVOLVEMENT*

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GRANULOMA inguinale is a chronic specific granulomatous infection, chiefly of skin and subcutaneous tissues. The lymph nodes are rarely involved. The selectivity of the disease for the genitalia has earned it a place in the category of venereal diseases.[1]

The condition was first described by McLeod in 1882; later, Conyers and Daniels (1896) reported such an entity in British Guiana. It occurred chiefly in young Negresses.

In the United States the disease has been endemic in the South and unrecognized for many years, but has been diagnosed more frequently since 1926.

The primary purpose of this paper is to emphasize that there can be bone involvement of an osteomyelitic nature produced by granuloma inguinale.

A review of the German literature discloses that Kuhn in 1906 described a patient with involvement of bones, liver, and spleen as did Hoffman in 1920. Thierfelder, in 1924, referred to occurrence of polyarthritis deformans in granuloma inguinale. In 1925 he described a patient with involvement of joints and skull.

Review of the American literature from 1926 onward reveals increasing awareness of the possibility of skeletal involvement by granuloma inguinale. Fox,[4] in 1926, reported 150 cases of granuloma inguinale indicating a 6 per cent involvement of the osseous structures.

In 1944, Paggi and Hull[5] reported a case of a 21 year old Negro man with metastatic osteolytic lesions involving the left clavicle, right scapula, right 6th rib and right 10th rib. Chen *et al.*,[3] in 1948, reported cases of extragenital involvement, sites of metastasis including cheek, neck, nose, throat, mouth, lips, larynx, gums, palate, and various osseous lesions.

The latest case, reported by Rajam *et al.*[6] in 1954, was a patient with involvement of the right tibia, clavicle, and right sacroiliac joint.

Ulcerations most frequently appear on the genitalia and in the inguinal regions. The initial lesion is usually in the form of a small macule which develops into a papule; then ulcerates, resulting in granulomatous ulceration. Spread is by continuity, autoinoculation, lymphatic or hematogenous means. Hematogenous spread results in osseous lesions. The disease is a slow, progressive debilitating process accompanied by fever, anemia, weight loss, malaise, and mild leukocytosis.

The disorder is to be differentiated from syphilis, chronic streptococcic ulcers, giant chancroids, and lymphogranuloma venereum. The slow but progressive character of the lesions, absence of a positive Wassermann reaction, and the lack of lymph node involvement should serve to prevent confusion. The final diagnosis rests on demonstration of Donovan bodies.[7]

Donovan bodies represent a pleomorphic coccobacillus, *Donovania granulomatis*, usually located within monocytes, although at times, smaller numbers are extracellular. Wright's method of staining usually reveals the Donovan bodies.[2]

The over-all incidence of osseous involvement appears to be approximately 6 per cent of all cases encountered. Bone involvement is well known, but has not been stressed as a complication of the disease.

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* This material has been received by the Office of The Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any indorsement of the opinions advanced or any recommendation of such products as may be named.

† Chief, Radiology Service, Letterman General Hospital, San Francisco, California.

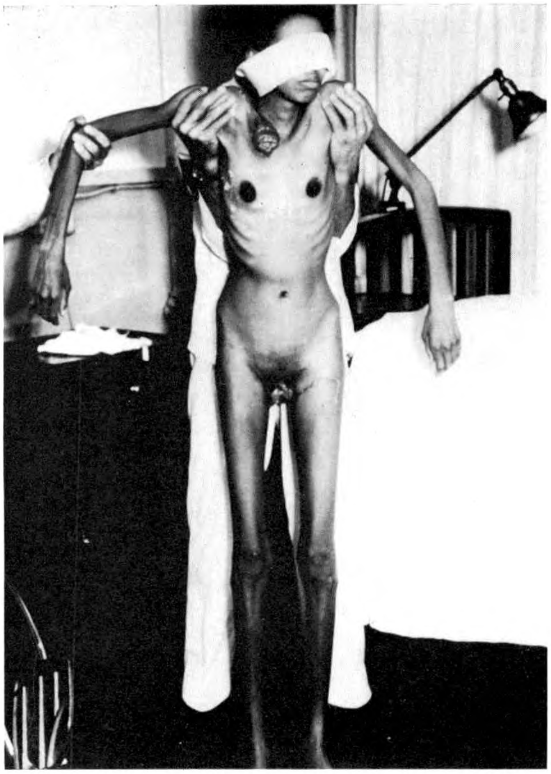

Fig. 1. Photograph of patient on admission.

REPORT OF A CASE

History of Present Illness: The patient was a 19 year old Negro woman who was well until the last week in December, 1957, when she noted a small nodular lesion on the perineum. Approximately 2 weeks later a similar lesion appeared on the anterior left chest. These lesions increased markedly in size and drained purulent material. There was associated anorexia, malaise, and a 60 pound weight loss in 2 months. The patient weighed 140 pounds in November, 1957, and 80 pounds on admission to the hospital in April, 1958.

Past History: The patient had no previous lesions. There was one pregnancy which terminated in spontaneous abortion in March, 1957. The patient's last pelvic examination was in July, 1957, and was said to be normal.

Physical Examination on Admission: The patient appeared chronically ill, cachectic, demonstrated evidence of marked weight loss, and was so weak that she could not stand (Fig. 1). There was a red, beefy, velvety fungating mass, measuring 2.5 cm. by 3.5 cm., on the right anterior chest overlying the proximal end of the right clavicle. This mass bled easily when traumatized and was covered with foul smelling, purulent exudate (Fig. 2). There was a similar lesion of the perineum, extending from the pubis to the sacrum (Fig. 3). The remainder of the physical examination was within normal limits.

Laboratory and Roentgenographic Studies: Results of urinary studies were negative. The patient's white blood cell count was 26,300 with 84 per cent polymorphonuclear cells, 15 per cent lymphocytes and 1 per cent eosinophils. The red blood cell count was 4.4 million. Hemoglobin was 12 gm. per cent. Repeated differential cell counts throughout the hospital course demonstrated a persistent leukocytosis in the range of 20,000 to 30,000 cells. On February 24, 1958 Donovan bodies were seen on smears of aspirated material from the lesions of

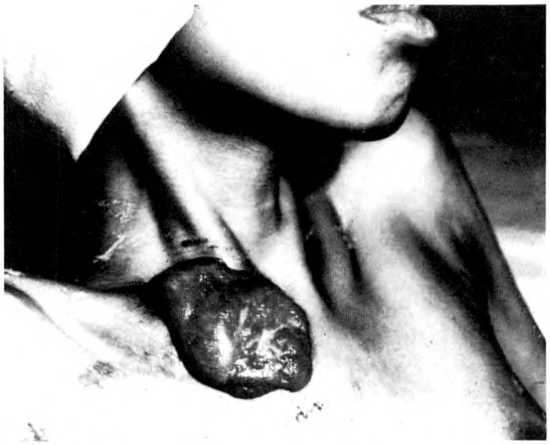

Fig. 2. Lesion on right anterior chest over proximal end of right clavicle.

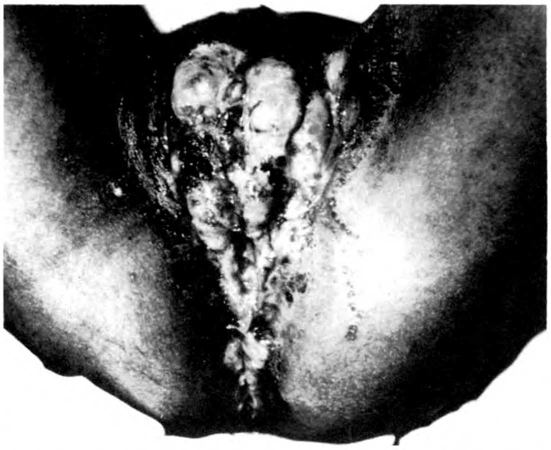

Fig. 3. Lesion of perineum from pubis to sacrum.

the clavicle and perineum. Roentgenograms were diagnostic of a large soft tissue mass overlying the proximal end of the right clavicle, with areas of osseous destruction and slight expansion of the proximal end of the clavicle (Fig. 4). No other abnormalities were noted in the skeletal survey.

Treatment: Cases reported early in the literature were treated with tartar emetic and fuadin with little or no results. Sulfa drugs were then used, particularly sulfadiazine, with no improvement. At times, amputation was utilized if the extremities were involved—treatment given as for osteomyelitis. Recently, terramycin has become the drug of choice.

This patient was given terramycin, 2 gm. daily for 30 days. She also received supportive treatment, vitamins and ferrous sulfate, and local cleansing of the skin lesions with hydrogen peroxide. During this period the patient's weight increased from 80 pounds to 110 pounds. She became ambulatory and there was approximately a 50 per cent clearing of the lesions of the perineum and chest. After 30 days of terramycin therapy, the patient was discharged, to be seen in the Out-Patient Clinic. Studies for Donovan bodies were negative at this time.

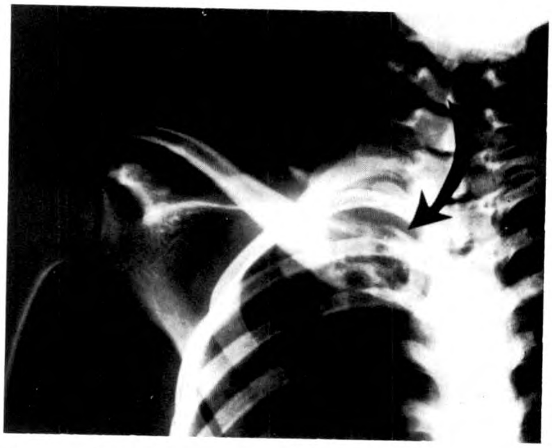

Fig. 4. Roentgenogram showing soft tissue mass and osseous destruction with expansion of clavicle.

Close follow-up of this patient showed that all lesions of the skin and the osseous lesion of the right clavicle had healed 4 months after discharge.

SUMMARY

Granuloma inguinale is a chronic granulomatous infection resulting from invasion by a pleomorphic coccobacillus, *Donovania granulomatis*. It chiefly involves skin and subcutaneous tissues but also may spread via the blood stream, resulting in osteomyelitic findings roentgenographically; such a case and its treatment is recorded in this paper, including a review of the literature pertaining to this entity.

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EDITORIAL

UROLOGICAL DIAGNOSIS—PAST AND PRESENT

> *"Things don't turn up in this world*
> *until somebody turns them up"*
> Garfield

ALL radiographic diagnosis is of necessity based upon observation, detection, and interpretation. The evolution of diagnostic techniques is broadly due to man's ingenuity and imagination. From the time of the original disclosures of Wilhelm Conrad Röntgen, men of vision, chiefly physicists, physicians, chemists, engineers, inventors and manufacturers, have strived for more precise methods and materials as aids in x-ray diagnoses. Since the physiology of the urinary tract lends itself admirably to radiographic investigation, this system has been a natural target for continued research. The result is that today we have many methods by which an extremely accurate evaluation of all portions of the urinary tract in health and disease is possible.

Pioneers in the development of radiopaque drugs for use in excretory urography: Rowntree, Swick, Binz, Rath and others, had visions far beyond the observation of a survey film for stone. Edison, Coolidge, Paterson, Fuchs, Dodd, Machlett and Baetjer, to mention only a random few who were responsible for early x-ray procedures, had visions of radiographic equipment and techniques far beyond the single static roentgenogram of the kidneys. From such men, the torch of progress has been carried by younger generations to give us our present methods for the visualization of the perirenal soft parts, renal excretory pathways, arteries, veins, ureters, bladder, and urethra. These structures can now be visualized in single, multiple, rapid serial or cinegraphic combination, with or without stereoscopy or tomography. With all this now available, one wonders in which direction future research in this area can be directed. Perhaps improvements of presently available methods can be expected rather than the discovery of new procedures.

In addition to the pictorial or radiographic studies, chemists, physiologists, physicians, and engineers have combined efforts to functionally evaluate the urinary tract, particularly the renal mass. Early rapid serial film exposures during intravenous pyelography for differential nephrographic evaluation has become standard in certain groups of patients. The urea washout test is now recommended in the hypertensive patient with suspected renal or renal vascular disease. The inherent value of this test seems to be one of simplicity and clarity of definition of the shadows on the roentgenogram. The use of larger than average amounts of radiopaque material for the demonstration of the kidneys in those patients who have diminished renal function is an outgrowth of experience with arterial or venous injections for angiocardiography and aortography. As much as five times the regularly recommended dose of radiopaque material may safely be injected in those patients by the intravenous drip method. In this manner, satisfactory excretory pyelograms may be obtained in a group of seriously ill patients who otherwise might necessarily be subjected to the more serious procedure of retrograde pyelography. The use of radioisotope renograms and renal scanning for the functional study of renal components has now become recognized as a valuable method for routine clinical practice.

All of these diagnostic procedures which utilize the differential density of the combined iodine molecule have an inherent hazard, which is usually considered as an allergy or a colloidal shock reaction. Side effects of this may be mild, severe, or fatal. Fortunately, the newer radiopaque media, although not without danger, seem somewhat less hazardous when applied with proper clinical judgment. At least, we have learned to anticipate and promptly treat these reactions when they occur, although we cannot predict which patient will react unfavorably. The significant factor is the evaluation of this potential danger during these procedures versus the clinical need or benefits to be derived. Unnecessary diagnostic tests of this type can only be condemned. Sometimes the exercise of clinical judgment can be even more rewarding than an x-ray picture. Since most tests for allergy do not apply to drug reactions, the best one, at present, seems to be the intravenous test dose. Some recent animal experiments would indicate that clumping of red blood cells in end vessels, particularly in the pulmonary circulation producing multiple small emboli, results in a nonallergic shock syndrome. This type of reaction can be prevented by intravenous dextran solution. It is now reasonable to assume that more than one factor is present as a cause of "reactions" to radiographic drugs. The clinician must be alert to differentiate and to promptly treat the patient in this emergency.

A significant number of surgically correctable lesions of the renal artery may be detected by selective arteriography. It would appear that a new breed of radiologist is being trained to perform these studies either as a part of a team or as an entire team. The availability of the modern fluoroscope with image amplifier and television or cineradiography has been of great value in this type of study. The advantages of retroperitoneal pneumography prior to exploratory surgery have been well documented. Once a hazardous procedure, the present method using CO_2 as a contrast medium has proven safe and satisfactory in selected instances.

In the study of motion, perhaps the most useful clinical information has been derived from cineradiography of the vesical neck and urethra in children. Those who have employed this procedure are enthusiastic, but unfortunately many practicing radiologists or urologists are not yet able to avail themselves of the necessary equipment. Our present knowledge of bladder and bladder neck dysfunction is quite limited. More extensive use of such physiologic motion studies is certainly warranted in the future.

Progress in the diagnosis of urinary tract disease continues and fertile fields for further investigation are unfolded. As our knowledge and skills increase in this area, so will mankind benefit in return.

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NEWS ITEMS

CARL V. S. PATTERSON CHAIR IN CHEMICAL ENGINEERING

The establishment of the Carl V. S. Patterson Chair in Chemical Engineering in the University of Pennsylvania's School of Chemical Engineering has been announced by Dr. Gaylord P. Harnwell, President of the University.

The professorship will be supported by a bequest from the late Mr. Patterson, who was graduated from the University's School of Chemical Engineering in 1911. This is the first fully endowed professorship to be established in chemical engineering.

Mr. Patterson was the developer of the x-ray intensifying screen. He was born in 1888 in Wysox Township, Pennsylvania and died this past April.

Mr. Patterson began his research in fluorescence in 1912, in the employ of the Snook Roentgen Manufacturing Company in Philadelphia. In 1914, he went to Towanda and set up a laboratory for further research in this same field. He produced the first x-ray intensifying screens in 1916, and in 1925 the Patterson Screen Company was incorporated. In 1936, the firm began developing phosphorus powder for incandescent light bulbs, and in 1941 the Sylvania Electric Products Company purchased Mr. Patterson's phosphors plant. His screen company was sold to E. I. du Pont de Nemours and Company, Inc., in 1943 and became a division of du Pont's Photo Products Department. Mr. Patterson served as division manager until his retirement in 1950.

Carl V. S. Patterson had long been active in business, civic and welfare organizations. He was a member of Sigma Xi, an honorary scientific fraternity, and was active in University alumni affairs during his life.

PROFESSOR W. V. MAYNEORD HONORED

The Royal Swedish Academy of Science awarded its gold medal "Pro Meritis Protectione Contra Radiationem" to Professor W. V. Mayneord in 1965. The medal was presented to Professor Mayneord at the Eleventh International Congress of Radiology, which was held in Rome, September 22–28, 1965.

Until his retirement in September, 1964, Professor Mayneord held the position of Professor of Physics as applied to Medicine at the University of London, and he was Director of the Department of Physics at the Institute of Cancer Research, Royal Cancer Hospital, London. He was a member of the International Commission on Radiological Protection from 1950 to 1959; from 1950 to 1956 he was Chairman of the Commission's committee on protection against high energy radiations.

HARVEY PICKER NAMED TO NATIONAL SCIENCE BOARD

Harvey Picker, president of Picker X-Ray Corporation, has been appointed by President Johnson to serve on the National Science Board.

The board, composed of prominent scientists outside the government, is charged with studying the nation's scientific needs and recommending national policies and programs for promoting research and education.

CONTINUATION COURSE IN ROENTGENOLOGY OF CHEST DISEASES

The University of Minnesota and the Department of Radiology announce a continuation course in Roentgenology of Chest Diseases, which will be held October 25–29, 1965, in the Mayo Memorial Auditorium at the University of Minnesota Medical Center on the Minneapolis Campus.

The course is designed for radiologists and others interested in the field of chest diseases. It will cover the procedures presently available in the radiologic field for diagnosing chest diseases with background discussions on the rationale of utilizing these procedures. The course will also provide basic information of the anatomy and physiology of the thorax and its contents, as well as discussions on the pathology of various diseases of the chest.

Guest participants will include Drs. Felix G. Fleischner, Boston, Massachusetts; Robert G. Fraser, Montreal, Quebec, Canada; L. Henry Garland, San Francisco, California; Ted F. Leigh, Atlanta, Georgia; Averill A. Liebow, New Haven, Connecticut; John F. Murray, Los Angeles, California; Sidney W. Nelson, Columbus, Ohio; Leo G. Rigler, Los Angeles, California; and George Simon, London, England.

The course will be presented under the direction of Drs. Harold O. Peterson, Professor and Head, John A. Tobin, Assistant Professor, and Eugene Gedgaudas, Assistant Professor, Department of Radiology. The remainder of the faculty includes members of the teaching staff of the University of Minnesota Medical School and the Mayo Graduate School of Medicine, Rochester, Minnesota.

An interesting series of tours to historical, cultural, and scenic places has been arranged by the Radiology Wives Club for the wives of registrants attending the course. Further information will be sent at the time of acknowledgement of registration.

Those interested may write to the Director, Center for Continuation Study, University of Minnesota, Minneapolis, Minnesota 55455.

GASTROENTEROLOGICAL CONVENTION

The 30th Annual Convention of the American College of Gastroenterology will be held at the Americana Hotel in Bal Harbour, Florida, October 25–27, 1965.

In addition to the individual papers to be presented, there will be a Panel Discussion on Diseases of the Pancreas and a Photoquiz on Gastroscopy in which several authorities and the audience will participate. A Wednesday evening session devoted entirely to a Radiology Ouiz, will be conducted by Dr. Manuel Viamonte, Jr., of Miami, Florida, and others as participants.

Foreign speakers include Dr. John Tomenius of Sweden, Dr. Vinko Percic of Yugoslavia, and Dr. Zdenek Maratka of Czechoslovakia, amongst others.

On October 28, 29 and 30, immediately following the Convention, the Annual Course in Postgraduate Gastroenterology will be given.

Copies of the program and further information may be obtained by writing to: American College of Gastroenterology, 33 West 60th Street, New York, N.Y. 10023.

SECTION OF RADIOLOGY, SOUTHERN MEDICAL ASSOCIATION

The 59th Annual Meeting of the Southern Medical Association will be held in Houston, Texas, November 1–4, 1965.

The Section on Radiology has a very informative program prepared. The highlights of this program are as follows:

1. Two Panel Discussions held jointly with the Sections on Pathology and Surgery. The Panel Discussions will be on "The Modern Evaluation of Breast Disease and the Role of Mammography" and "A New Look at Lymphomas and the Value of Lymphangiography."
2. There will be four Refresher Courses given by Drs. Philip Rubin, Gershon-Cohen, and Viamonte on the following subjects: "Bone Dsyplasias," "Mammography," "Thermography," and "The Roentgenologic Manifestations of Abnormal Pulmonary Vasculature."
3. This year's Guest Speaker will be Dr. Philip Rubin, Chief and Professor of Radiotherapy, University of Rochester School of Medicine, Rochester, New York. Dr. Rubin will participate in the Panel Discussion on Breast Disease and will give the Guest Speaker's Address on "The Problems of the Solitary Metastasis."

Those interested in attending this meeting should apply directly to the SMA Housing Bureau, 1006 Main Street, Suite 1101, Houston, Texas 77002.

SYMPOSIUM ON CLINICAL ASPECTS OF HODGKIN'S DISEASE

The latest clinical and research information on Hodgkin's disease will be presented at a Symposium, co-sponsored by the American Cancer Society and the National Cancer Institute, to be held Monday, November 22, 1965 in the Sutton Ballroom, at the New York Hilton Hotel in New York City.

The morning session beginning at 9:30 A.M. will be moderated by Dr. Kenneth Endicott, Director, National Cancer Institute, and will have as Speakers: Dr. John E. Ultmann, New York, New York; Dr. Alan Aisenberg, Boston, Massachusetts; Dr. Robert J. Lukes, Los Angeles, California; and Dr. M. Vera Peters, Toronto, Ontario, Canada.

The afternoon session will begin at 2:00 P.M. and Dr. Leonard Larson, President, American Cancer Society, Inc., will act as moderator. The Speakers at this session will be: Dr. Henry S. Kaplan, Palo Alto, California; Dr. David A. Karnofsky, New York, New York; Dr. Emil Frei, III, Houston, Texas; Dr. James T. Grace, Buffalo, New York; and Dr. Eric C. Easson, Manchester, England.

Dr. Sidney Farber of Boston, Massachusetts, will present a summary and the conclusions of the Symposium.

For further information, write: Dr. Jack W. Milder, Research Department, American Cancer Society, Inc., 219 East 42 Street, New York, New York 10017.

THIRD INTERNATIONAL CONFERENCE ON HYPERBARIC MEDICINE

The Third International Conference on Hyperbaric Medicine, sponsored by Duke University Medical Center and the National Academy of Sciences—National Research Council, will be held November 17–20, 1965 at Duke University, Durham, North Carolina.

An outstanding program has been arranged.

The main topics to be discussed include the following: Wednesday A.M., "Oxygen and Cellular Metabolism"; Wednesday P.M., "Oxygen Toxicity"; Thursday A.M., "Physiologic Responses to High Oxygen Tension" (2 sessions); Thursday P.M., "Hyperbaric Oxygenation in Cardiovascular Disease" (2 sessions); Friday A.M. and P.M., "Hyperbaric Oxygenation in Anaerobic Infections" (2 sessions); Friday P.M., "Hyperbaric Oxygenation and Radiation Therapy"; and Saturday A.M., "Hyperbaric Oxygenation in Treatment of Certain Toxemias and in Tissue Preservation."

The topic on Radiation Therapy will be moderated by Dr. J. A. del Regato, Department of Radiology, The Penrose Cancer Hospital, Colorado Springs, Colorado. The participants will be Dr. H. A. S. van den Brenk and Dr. N. Sparrow, Cancer Institute Board, Melbourne, Australia; Dr. I. Churchill-Davidson, Department of Radiation Therapy, St. Thomas' Hospital, London, England; Dr. R. J. R. Johnson, Department of Radiation Therapy, Winnipeg General Hospital, Winnipeg, Manitoba, Canada; Dr. Orliss Wildermuth, Department of Radiation Therapy, Swedish Hospital, Seattle, Washington; Dr. John T. Mallams, Department of Radiology, Baylor University Medical Center, Dallas, Texas; and Dr. Fernando Bloedorn, Department of Radiology, University of Maryland School of Medicine, Baltimore, Maryland.

On Saturday afternoon, November 20, immediately after the closing session of the Conference, a football game will be played in Duke University Stadium between Duke University and The University of North Carolina. This game between traditional rivals is a yearly classic.

For further information contact the Secretariat, Box 2928, Duke University Medical Center, Durham, North Carolina.

BOOK REVIEW

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

THE SCIENCE OF IONIZING RADIATION: MODES OF APPLICATION. Edited by Lewis E. Etter, B.S., M.D., F.A.C.R., Professor of Radiology, Western Psychiatric Institute and Clinic and the Falk Clinic, School of Medicine, University of Pittsburgh, Pittsburgh, Pa.; Consultant, C. Howard Marcy State Hospital, Pittsburgh, Pa. Cloth. Pp. 788, with many illustrations. Price, $26.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1965.

The editor has enlisted the help of 35 contributors in compiling this book on the modes of application of radiation.

The First American Congress of Radiology, in a unique meeting in Chicago, Illinois, in 1933, appointed a Committee on History and Education whose assignments included "the editing of a book which would denote the outstanding features developed in the science of Radiology from the time of Roentgen's discovery to the period of the Congress."

That same year, an impressive work entitled "The Science of Radiology" was published. This comprehensive survey contained 25 chapters of articles dealing with the discovery of x-rays and radium; the American pioneers in radiology; roentgen and radium physics; radiologic diagnosis and therapy; x-ray and radium dosimetry; radiobiology; the teaching of radiology; and information about radiologic societies and literature. The nature of cosmic, ultraviolet, light, infrared and mitogenetic radiations was also discussed.

No Second American Congress of Radiology was every organized and no further edition of The Science of Radiology was published.

In the present book, "The Science of Ionizing Radiation," an up-dating of the science of radiation is made in a remarkable presentation.

In the last 30 years, the science of ionizing radiation has expanded and has become a multifaceted subject. That there has been tremendous progress in the general production and use of ionizing radiations is borne out by comparing the 1933 text of The Science of Radiology and the present text of The Science of Ionizing Radiation.

There are 14 main sections in this book: History, Equipment, Physics, Media and Screens, Chemistry, Radiobiology, Human Diagnostic and Therapeutic Applications, Industrial Use, Crystallography, Paleontology-Archaeology, Anthropology, Graphic Arts, Agriculture and Protection, comprising 29 chapters.

The chapters are well-balanced, representing comprehensive reviews on the subject. Among them, the chapters on the Natural Radioactive Element Therapy of Malignant Disease, the Physics of Radiation, the History of Roentgen Rays and Radium, and the Radioactive Isotope Use of Diagnosis and Treatment are particularly outstanding.

Although primarily intended for radiologists, the general scientific public should also find this book of great value. As a reference source, this beautifully produced volume will be helpful to those working in physics, biology, chemistry, anthropology, and archaeology.

There is a useful index of authors and subjects. The references are complete, the illustrations are of excellent quality and the general editing by Dr. Etter is eminently authoritative. This reviewer is enthusiastic and recommends *The Science of Ionizing Radiation* without hesitation.

RICHARD C. PFISTER, M.D.

BOOKS RECEIVED

RADIOLOGIC STUDIES OF THE GRAVID UTERUS. By Paul A. Bishop, M.D., Consulting Radiologist, Pennsylvania Hospital; formerly, Director of the Department of Radiology, Pennsylvania Hospital, and Chief of Radiology of its Benjamin Franklin Clinic; Professor of Radiology, School of Medicine, and Professor of Radiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia; with a foreword by Robert A. Kimbrough, M.D. Cloth. Pp. 279, with 250 illustrations. Price, $14.50. Harper & Row, Publishers, 49 East 33rd Street, New York 16, N.Y., 1965.

DENTAL RADIOLOGY. By William Ward Wainwright, D.D.S., M.S., F.A.C.D., F.A.A.A.S., F.I.C.A.N.;

Diplomate of the American Board of Oral Medicine; Diplomate of the International Board of Applied Nutrition; with a foreword by George M. Hollenback, D.D.S., M.S., D.Sc., F.A.C.D., F.A.A.A.S. Cloth. Pp. 585, with many illustrations. Price, $17.50. McGraw-Hill Book Company, 330 West 42nd Street, New York, N.Y. 10036, 1965.

THE ROENTGEN DIAGNOSIS OF TRAUMA. By Herbert R. Zatzkin, M.D., F.A.C.R.; Chairman, Department of Radiology, Meadowbrook Hospital, the Nassau County Public General Hospital, East Meadow, Long Island, New York; Consultant Radiologist, Community Hospital, Glen Cove, New York; Consultant Radiologist, Hempstead General Hospital, Hempstead, New York; and Consultant Radiologist to the Office of the Medical Examiner, Nassau County, New York. Cloth. Pp. 448, with 591 illustrations. Price $22.00. Year Book Medical Publishers, Inc., 35 East Wacker Drive, Chicago, Ill. 60601, 1965.

A TEXTBOOK OF ELEMENTARY RADIOGRAPHY FOR STUDENTS AND TECHNICIANS. By Donald deForest Bauer, M.D., C.M., M.Sc., D.A.B.R.; Associate Radiologist, Klamath Valley Hospital and Presbyterian Intercommunity Hospital; Associate Professor of Medical X-Ray Technology, Oregon Technical Institute, Klamath Falls, Oregon; Radiologist at Modoc Medical Center in Alturas and Cedarville, California; and with a foreword by Benjamin Goldberg, M.D., D.A.B.R.; Radiologist, Good Samaritan Hospital, Corvallis, Oregon; Radiologist, Lebanon Community Hospital, Lebanon, Oregon; and Honorary Member, Oregon Society of X-ray Technicians. Cloth. Pp. 242, with some tables. Price, $8.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1965.

THE SAGITTAL DIAMETER OF THE SPINAL CORD AND SUBARACHNOID SPACE IN DIFFERENT AGE GROUPS: A ROENTGENOGRAPHIC POST-MORTEM STUDY. By Lars Nordqvist. Paper. Pp. 96, with many illustrations. Acta Radiologica Supplementum No. 227. Acta Radiologica, Stockholm 2, Sweden, 1964.

BONE RESORPTION IN CASES WITH COMPLETE UPPER DENTURE: A QUANTITATIVE ROENTGENOGRAPHIC-PHOTOGRAMMETRIC STUDY. By Lennart Wictorin. Paper. Pp. 97, with some illustrations. Acta Radiologica Supplementum No. 228. Acta Radiologica, Stockholm 2, Sweden, 1964.

IRRADIATION OF LYMPH NODES AND VESSELS: EXPERIMENTS IN RATS, WITH REFERENCE TO CANCER THERAPY. By Arnfinn Engeset, M.D. Paper. Pp. 125, with many illustrations. Acta Radiologica Supplementum No. 229. Acta Radiologica, Stockholm 2, Sweden, 1964.

ACTIVATION OF THE FIBRINOLYTIC SYSTEM IN HUMAN BLOOD BY STREPTOKINASE AND CHANGES IN THIS SYSTEM AND IN THE EUGLOBULIN CLOT LYSIS TIME IN RELATION TO AGE AND SEX. By Yrjö P. Konttinen. Paper. Pp. 111, with some figures. The Scandinavian Journal of Clinical & Laboratory Investigation, Volume 17, Supplementum 82, Helsinki, 1965.

ABSTRACTS OF RADIOLOGICAL LITERATURE

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ROENTGEN DIAGNOSIS

Head

Hoefnagel, D., and Benirschke, K. Dyscephalia mandibulo-oculo-facialis (Hallermann-Streiff syndrome). *Arch. Dis. Childhood*, February, 1965, *40*, 57–61. (From: Departments of Pathology and Pediatrics, Dartmouth Medical School, and Department of Pediatrics, Hitchcock Clinic, Hanover, N. H., Department of Pediatrics, Boston City Hospital, Boston, Mass., and Laconia State School, Laconia, N. H.)

Three cases of one of the more rare forms of cranio-facial dysostosis are reported. This form is referred to as dyscephalia mandibulo-oculo-facialis. Other cases have been described under a variety of names among which are Hallermann-Streiff, François, Ullrich and Fremery-Dohna syndromes.

The patients reported are infants, 2 females and 1 male, 12 months, 3 months, and 5 months of age respectively. Outstanding features of the syndrome are skull and face abnormalities, dental anomalies, localized hypotrichosis, congenital eye malformations, dwarfism, and motor and mental retardation.

The clinical appearance of these patients is striking. The skin of the face and scalp, especially over the nose, is white, thin, and tense with many small blood vessels visible. There is diminished hair growth on the scalp. The nose is small and beaked with a sharp nasal frontal angle. Fully erupted teeth may be present at birth. The anomalies of the eye include bilateral microphthalmia, congenital cataract, ocular nystagmus, and strabismus. The body growth is retarded in most cases resulting in proportionate dwarfism with retarded bone age. Motor, mental, and speech development are usually also retarded.

The roentgen features of this rare syndrome are brachycephalic skull, prominent frontal and parietal eminences, and delayed closure of the anterior and posterior fontanelles. In some cases a shallow sella turcica, platybasia, and increased digital markings have been noted. The zygomatic processes may be hypoplastic but the most impressive change in the facial skeleton is mandibular hypoplasia with deformities or absence of the temporomandibular joint.

Male and female cases have been reported with equal frequency. With few exceptions the patients have resulted from normal pregnancies and have been normal at birth. Sex chromatin and chromosome studies in a very limited number of cases have not revealed any consistent abnormalities.

The syndrome described above superficially resembles progeria, mandibulo-facial dysostosis, and cleidocranial dysostosis.—*Gerald J. Kurlander, M.D.*

Pansini, R., and Lurà, A. Contributo clinico-radiologico sulla "disostosi cleido-cranica" di Pierre-Marie, Sainton, Crouzon. (Clinical and radiologic study of "cleido-cranial dysostosis" of Pierre-Marie, Sainton, Crouzon.) *Ann. radiol. diag.*, 1964, *37*, 275–303. (From: Istituto di Semeiotica Medica dell' Università di Ferrara and Istituto di Radiologia dell'Università di Ferrara, Italy.)

After an exhaustive review of the literature, the authors present 2 cases of cleido-cranial dysostosis and describe in detail the skeletal changes characteristic of the disease.

The skull is large, asymmetric and branchycephalic. The frontal bosses are prominent. There is a dehiscence of the metopic and lambdoidal sutures and a persistance of the fontanelles. Numerous wormian bones and the prominent diploic channels constitute the "mosaic skull" of Debré-Lamy-See. The inner table of the calvarium is thickened, the outer table thinned. There is evidence of platybasia, hypertelorism and exophthalmus.

The maxilla is frequently involved. A split palate may be present. The mandible may develop normally but when there is a retardation in the closure of the symphysis mentis, the mandibular angle is widened and the coronoid apophyses are shortened. These changes produce a prognathism. A marked disturbance of decidual and of permanent dentition takes place.

Dysostosis of the clavicle is pathognomonic and the result of retarded or of incomplete development of the three centers of ossification. The clavicular malformations are variable. They may be unilateral, bilateral, symmetric or asymmetric. They may be represented by angulations, thickenings, pseudoarthroses, aplasia.

Alterations of the pelvis and of the extremities are often observed, *i.e.*, dysplasia of the pubic bones and of the coxo-femoral articulations, congenital subluxation of the hip, coxa vara, genu valgum, brachydactyly, syndactyly and clinodactyly.

The spine is frequently affected, the changes consisting of kyphosis, scoliosis, exaggerated lordosis, hemivertebrae, spina bifida and cervical rib.

The authors conclude that: (1) The dysostosis does not only involve bones of membranous origin but also those formed in cartilage; (2) it is probably the result of an embryonal mesenchymal disorder; and (3) although its transmission occurs in accordance with dominant mendelian characteristics, there is no evidence of deviations from the normal chromosome constitution.—*Anthony A. Blasi, M.D.*

Mellick, S. A., and Phelan, P. D. Internal carotid artery occlusion in a child. *Arch. Dis. Childhood*, April, 1965, *40*, 224–226. (From:

Princess Alexandra Hospital, Brisbane, and Department of Child Health, University of Queensland, and Brisbane Children's Hospital, Brisbane, Australia.)

Occlusion of the internal carotid artery is a rare condition in children. The authors' review of the literature revealed 29 cases reported since 1960.

They report a case of a 7 year old boy with episodes of transient left hemiplegia and right-sided headaches. There were the physical findings of weak right carotid pulse, a bruit over the right carotid artery and the right frontal and temporal area, weakness of the left leg, and positive left Babinski response. Skull roentgenography showed slight under-development of the right side, and a right carotid angiogram demonstrated good filling of the external carotid artery and its branches, but no filling of the intracranial branches of the internal carotid and gradual tapering of the cervical portion of this artery. The serum cholesterol level was normal.

When the symptoms became worse, 4 months later, an operation was performed and an atheromatous plaque was palpable and visible in the proximal 1 cm. of the internal carotid artery and beyond this the artery was about 2 mm. in external diameter. An arteriotomy through the region of the plaque, and widening of the vessel with a patch graft, resulted in clinical improvement of what appeared to be progressive deterioration.

This is the first reported case of a childhood carotid artery occlusion with a typical atheromatous patch as the underlying cause. Atheroma is very rare in children, particularly in the absence of hypercholesterolemia. Previously reported cases of carotid occlusion were the result of injury in the region of the soft palate, severe throat infection, thrombosis of a patent ductus, and calcification of the arterial wall, but in the majority of cases no definite pathology could be found.—*James R. Knapp, M.D.*

Matsuba, Michio, Ichii, Shogo, and Kobayashi, Shigeru. Effect of head irradiation with x-rays on cholesterol side chain cleavage activity in rat testes. *Jikei Med. J.*, July, 1964, *11*, 97–99. (From: Department of Pharmacology, The Jikei University School of Medicine, Tokyo, Japan, and the Department of Physiology and Pathology, The National Institute of Radiological Sciences, Chiba, Japan.)

It is well documented that germinal cells of the seminiferous tubules are susceptible to ionizing radiation. The functions of the testicular interstitial cells are less well documented. The present article deals with the effects of irradiation of the head of the rat with roentgen rays to determine the activities of cholesterol side chain cleavage in the rat testes.

Four groups of rats were selected, each group consisting of 6 animals. The rats were placed within shielded capsules with only the head exposed to irradiation which was given in the dosage of 3,000 r. The animals were then sacrificed at 6 hours for the first group, 24 hours for the second group, 48 hours for the third group, and 72 hours for the fourth group. Studies of the testicle were then made to determine the activities of cholesterol side chain cleavage in them.

The presented results would suggest that release and/or production of pituitary gonadotropins might be increased at 6 hours after head irradiation of the rat, decreased between 24 to 48 hours postirradiation, and then increased again by 72 hours postirradiation.—*David C. Alftine, M.D.*

Kinersly, T., Jarabak, J. P., Phatak, N. M., and DeMent, Jack. (Portland, Oregon.) Laser effects on tissue and materials related to dentistry. *J. Am. Dent. A.*, Mar., 1965, *70*, 593–600.

Included in this report are a short review of the biologic laser literature, a description of laser action, some of the authors' experiments with lasers related to dentistry and a discussion of a few possible applications to dentistry.

Lasers convert light from incoherent to narrow coherent beams that can be focused by a variety of optical systems. The effective beam width can be reduced to one micron. The intensity of the laser beam can be adjusted.

Lasing has caused the bleaching of stained teeth and tooth sections. Sometimes this was accompanied by formation of chalky spots, craters, or small holes. The laser beam did not fuse powdered enamel and dentin. Stains increase the laser effect. Attempts at welding metals used in dentistry were not successful.

The intense heat spot produced by the laser may be useful in cauterizing or vaporizing oral soft tissue lesions.

Safety precautions for personnel are important when using lasers.—*Isaac Reese, M.D.*

Goldman, Leon, Gray, John A., Goldman, John, Goldman, Bernard, and Meyer, Robert. (Cincinnati, Ohio.) Effect of laser beam impacts on teeth. *J. Am. Dent. A.*, Mar., 1965, *70*, 601–606.

The authors describe a series of experiments in which extracted teeth were impacted by laser beams and one in which an intact tooth was lased before extraction. The teeth were studied grossly, microscopically, and microradiographically.

The studies indicate that considerable energy densities are required to produce changes in the enamel of normal teeth. Carious regions are more affected by the beam, this being especially true if the caries is colored, since the absorption is increased. Caries can be removed by the laser; it is not clear, however, whether the laser removes all of the caries.

When the laser beam was transmitted through a special glass rod to impact a right upper second molar in a patient, there was no sensation of pain. The transillumination caused by the laser beam through bone and soft tissue is of particular concern in lasing a patient.

In all procedures using lasers, safety precautions must be followed for the protection of both the patient and the operating personnel.—*Isaac Reese, M.D.*

NECK AND CHEST

CHAVANNE, C., PELLIER, D., and VALETTE, M. L'exploration radiographique des tumeurs du rhinopharynx; intérêt de la tomographie en incidence de Hirtz. (Radiographic exploration of rhinopharyngeal tumors; importance of tomography in the Hirtz position.) *J. de radiol., d'électrol. et de méd. nucléaire*, Jan.-Feb., 1965, *46*, 25–34. (From: Fondation Curie, Paris, France.)

Tomograms at 14 to 15 cm. from the vertex gave clearest visualization of the rhinopharynx in the experience of the authors. The patient, in a semi-recumbent position, rests the occiput on a horizontal head rest. The central ray is directed horizontally to the submental area, at 90 degrees to the plane of Reid, which is now parallel to the tomographic table which is placed vertically, the vertex of the skull touching it. Thus, in this position the patient does not hyperextend the neck as much as in the Hirtz position.

Roentgenograms taken during the Valsalva maneuver will visualize the rhinopharyngeal fossae better. For visualization of small and medium sized tumors of the rhinopharyngeal walls, the tomographic technique described above is indispensable in the opinion of the authors.

Several beautiful tomographic reproductions of such tumors are presented.—*Jirair N. Sarian, M.D.*

ROUSSEL, J., PERNOT, C., SCHOUMACHER, P., PERNOT, M., and KESSLER, Y. Considérations statistiques sur le cancer bronchique du mineur de fer du bassin de Lorraine. (Statistical evaluation of bronchial carcinoma among iron miners of Lorraine.) *J. de radiol., d'électrol. et de méd. nucléaire*, Oct., 1964, *45*, 541–546. (From: Centre anticancéreux de Lorraine, Nancy, France.)

A summary analysis of previous publications is given.

The authors then present a detailed study of bronchial carcinoma noted in 225 miners of iron (in Lorraine, France) as compared to 850 cases with the same disease found in other professions. A higher incidence of bronchial carcinoma is demonstrated among iron miners. Of the 225 cases, 194 could be clearly identified as to histopathology, whereas of the 850 nonminer cases, 768 could be so determined. Of the 194, 43.8 per cent had anaplastic carcinoma compared to 28.12 per cent of the 768 nonminer cases. In miners the epidermoid carcinoma constituted 52.6 per cent, whereas in the other groups this was 67.06 per cent. The incidence of adenocarcinoma was 3.6 per cent in iron miners and 4.82 per cent in the other professions. Thus there is definitely a higher ratio of anaplastic type of bronchial carcinoma among iron miners.

In miners the inferior lobes were somewhat more frequently affected, whereas in nonminers the upper lobes were definitely more often involved. A combination of hilar involvement with pneumoconiosis (compensatory emphysema) is by far the most common roentgen finding (43 out of 80 cases) among iron miners. Purely hilar involvement was noted in 18 out of 80 cases. Pneumoconiotic changes without hilar abnormality could be noted in 7 cases; 5 cases showed peripheral lesions (3 cases were mediastinal in appearance and 2 started with pleural manifestation).

The period of exposure to iron ore dust varied from 15 to 35 years, the average being 25.3 years. The average age was 54.4 years, whereas in nonminers this was 57.5 years. This difference is not significant statistically.

Cigarette smoking was found to be a factor in bronchial carcinoma in both the miners and nonminers to the same degree. Thus nonsmoking miners showed 1.55 per cent of carcinoma, whereas nonminers who did not smoke constituted 1.38 per cent of those affected with bronchial carcinoma. These ratios rose to 17.20 per cent in miners and 10.41 per cent in nonminers who smoked between 1 to 10 cigarettes a day. The figures were respectively 28.25 per cent and 33.05 per cent for those who smoked between 10 and 20 cigarettes a day, and were the highest (53.10 per cent in miners and 54.68 per cent in nonminers) for those who smoked more than 20 cigarettes a day. Miners of iron could smoke in the mines as compared to coal miners, for example, who could not smoke inside the mines because of explosion hazards.

The radioactivity in the iron mines was found to be less than the atmospheric radioactivity noted outside. Hence, radioactivity of the iron could not be assumed to be a cancerogenic factor.—*Jirair N. Sarian, M.D.*

MISENER, F. J., QUINLAN, J. J., and HILTZ, J. E. Hytrast: a new contrast medium for bronchography. *Canad. M. A. J.*, Mar. 20, 1965, *92*, 605–610. (From: Nova Scotia Sanatorium, Kentville, Nova Scotia, Canada.)

Hytrast, a mixture of two forms of diiodopyridone, was introduced in 1962 for use in bronchography. The advantages mentioned then, as listed by the present authors, were: (1) less alveolar filling; (2) rapid elimination from lung (2 to 7 days); (3) superior delineation of bronchial tree because of high iodine content and adhesive quality; and (4) less irritation than with other aqueous contrast agents.

Thirty-one bronchograms on 28 patients at Nova Scotia Sanatorium were done using hytrast. The diagnosis in 27 instances was tuberculosis; miscellaneous lung conditions accounted for the other 4. The contrast quality of the bronchograms was considered satisfactory. Good alveolar filling occurred in about half of the patients, minimal filling in 9, and appreciable filling in 6. Pyrexia of 100° to 102° F. was noted in 21 cases. Nausea occurred in 13 and vomiting in 6 instances. The authors believe that elimination of the hytrast from the lungs takes longer than 2 to 7 days.

Considering the quality of the roentgen studies, retention time in lungs after bronchography and the after-study reactions, the use of hytrast presented no real advantages over dionosil (oily) in this series. —*Newell K. Richardson, M.D.*

ROSENBAUM, HAROLD D. Roentgen demonstration of broken cardiac pacemaker wires. *Radiology*, May, 1965, *84*, 933–936. (From: Department of Radiology, University of Kentucky Medical Center, Lexington, Ky.)

Since 1960 thousands of cardiac pacemakers for long-term cardiac stimulation have been implanted for the treatment of Stokes-Adams attacks and to improve cardiac output in complete heart block. The most common complication following this procedure is a mechanical failure due to a broken wire leading from the pacemaker to or within the myocardium. As this diagnosis of a broken pacemaker wire is established by roentgenologic examination, the author feels it appropriate to report 3 examples recently at the University of Kentucky Medical Center, Lexington, Kentucky.

The only site of breakage seen at this institution has been at the junction where the bared electrode wires emerge from their insulating sheaths. Breakage is thought to be due to metal fatigue resulting from constant flexion which occurs not only from cardiac motion but also from breathing, bending, tying shoelaces, and numerous other normal activities.

Awareness by radiologists of this possible complication may hasten appropriate therapy, particularly in institutions where experience with this relatively new mode of treatment is limited.—*Donald N. Dysart, M.D.*

EDWARDS M., ALBERTO; SAAVEDRA V., JAIME; NOGUERA, HERNÁN; DEL CAMPO O., EMILIO; AHUMADA L., JORGE; and QUIROGA, JOSÉ. Angio cardiografía selectiva de cavidades izquierdas por vía transeptal. (Transseptal selective angiocardiography of left cardiac chambers.) *Enfermedades del torax y tuberc.*, 1963–1964, *28–29*, 46–52. (From: Hospital San Borja, Santiago, Chile.)

Retrograde arterial catheterization and direct puncture of the left cardiac chambers have been used to study the left side of the heart. Injections made through a catheter in the pulmonary artery have also been used to study the left side of the heart.

Through a venous catheter from below a transseptal needle may be introduced which will puncture the atrial septum so that pressures may be recorded and contrast material injected into the left atrium. The authors have used this method to study 10 patients with various valvular and congenital disorders. This is considered a method of choice for selective angiocardiography of the left atrium and some of the congenital lesions of the left side of the heart. It is second choice for left ventriculography when retrograde arterial catheterization is unsuccessful.—*Charles M. Nice, Jr., M.D., Ph.D.*

ARTUCIO, H., ESPASANDIN, J., FOLLE, L. E., DIGHIERO, J., and ZUBIAURRE, L. Coronariografia. (Coronariography.) *An. Fac. de med. de Montevideo*, 1964, *49*, 177–182. (From: Departamento de Cardiología, and Departamento de Radiología, Hospital de Clínicas, Montevideo, Uruguay.)

Coronary arteriography or coronariography is essential to study the pathology of the coronary circulation. Various methods have been proposed in which the contrast medium injected into the aorta just above the valve enters, according to the technique of Somes, into the coronary artery itself (selective coronariography). Roentgenography is accomplished by means of rapid filming or cinematography.

Ten patients were studied by the authors. The complications in general are those associated with catheterization or injection of iodine contrast agents. Electrocardiographic changes occur but are rapidly reversible. One patient had a ventricular fibrillation which necessitated a thoracotomy for defibrillation.

Preliminary results seem to show a good correlation between the anatomic findings and the clinical and electrocardiographic data. The procedures are regarded as preliminary to coronary surgery.—*Charles M. Nice, Jr., M.D., Ph.D.*

Sleight, Peter. Dissection of the aorta with pericardial tamponade: successful relief of tamponade. *Brit. M. J.*, May 1, 1965, *1*, 1165–1167. (From: Cardiac Department, St. George's Hospital, London, England.)

Dissection of the aorta is fatal in over 75 per cent of cases according to DeBakey and others. Rupture of the aorta is the commonest cause of death with the usual site of rupture into the pericardium. This causes death by cardiac tamponade.

The author reports a patient relieved surgically with improvement in her condition following diagnosis. This was a 79 year old woman who developed dissection of the aorta. The patient was operated on under local anesthesia and through the pericardium 200 ml. of bloody fluid was removed. The blood pressure immediately stabilized and the venous pressure became normal. The patient made an uneventful recovery and was discharged a few weeks later without symptoms.—*David C. Alftine, M.D.*

Boix-Ochoa, José, and Rehbein, Fritz. Oesophageal stenosis due to reflux oesophagitis. *Arch. Dis. Childhood*, April, 1965, *40*, 197–199. (From: Surgical Department of the Children's Hospital, Bremen, Germany.)

According to the authors, during childhood the majority of acquired esophageal strictures are due to gastro-esophageal reflux which is usually due to a hiatal hernia. However, minor forms of hernia and cardiac achalasia may cause a reflux that is so severe that esophagitis and subsequent stricture formation result.

In the Children's Hospital, Bremen, between 1954 and 1964, 226 hiatal hernias were operated upon, and of these 54 were complicated by stenosis of the esophagus. The result of treatment depends on the severity of the stricture. In the great majority of cases operative correction of the hiatal hernia and prolonged bouginage lead to successful results. When there is recurrence, colonic transplantation is performed.—*Arthur E. Childe, M.D.*

Lichter, Ivan, and Borrie, John. Intramural oesophageal abscess. *Brit. J. Surg.*, March, 1965, *52*, 185–188. (From: University of Otago, New Zealand.)

Intramural esophageal perforation with abscess formation may occur as a rare event following minor trauma to the esophageal mucosa. This permits infected material to gain access to the loose submucosa, producing a cylindrical dissection with extensive separation of the mucosa from the surrounding esophageal muscle.

The authors report 2 patients with intramural esophageal abscess, both of whom recovered following surgical drainage. They were females, one age 75 years and one age 53 years. The administration of contrast medium by mouth showed the appearance of a double barreled esophagus in the lower neck and the upper chest. It is felt that this appearance is pathognomonic of the lesion.

Both patients recovered following surgical drainage.—*Arthur E. Childe, M.D.*

Nix, Thomas E., Jr., and Christianson, Herbert B. Epidermolysis bullosa of the esophagus: report of two cases and review of literature. *South. M. J.*, May, 1965, *58*, 612–620. (From: Department of Dermatology, Ochsner Clinic, New Orleans, La.)

The authors report 2 patients suffering from epidermolysis bullosa who had severe esophageal stenosis as a result of this condition. There had been repeated blistering and scarring of this organ over the course of some years. Both patients died as a result of the disease.

Involvement of the esophagus in this condition is unusual, although involvement of the mucous membranes of the eyes, nose, oropharynx, anus and genital tract is a well-known feature.

Roentgenography with barium demonstrates the stenotic segment of the esophagus with smooth tapering conical margins at either end of the segment. Treatment consists of avoidance of rough or hot foods, esophageal dilatations for stenoses and surgical measures when indicated for severe complications.—*Arthur E. Childe, M.D.*

Carter, Richard, and Hinshaw, David B. Use of the esophagoscope in the diagnosis of rupture of the esophagus. *Surg., Gynec. & Obst.*, June, 1965, *210*, 1304–1306. (From: Department of Surgery, Loma Linda University School of Medicine and the Los Angeles County General Hospital, Los Angeles, Calif.)

Rupture of the esophagus is associated with a high mortality chiefly because of failure to make an early diagnosis. The diagnostic features of this condition are well enough known if this possibility is borne in mind.

An upright chest roentgenogram is the single best examination, but is occasionally negative. Barium study of the esophagus may also be negative. By adding "diagnostic error" to these truly negative examinations, it is apparent that the proper diagnosis is often not made, even though a classic history of rupture of the esophagus is present.

For this reason, esophagoscopic examination is recommended in suspect cases when other diagnostic studies prove to be negative.—*Richard E. Kinzer, M.D.*

ABDOMEN

Bloomberg, Max-Louis. Localized giant hypertrophy of the gastric mucosa with multiple polyposis (Menetrier's disease). *Canad. M. A. J.*, June 5, 1965, *92*, 1227–1229. (From: Eastern Hospital, Montreal, Quebec, Canada.)

Menetrier described giant hypertrophy of the gastric mucosa of the stomach in 1888. Since he also described multiple polyposis of the stomach, both conditions are commonly known as Menetrier's disease.

A patient with "localized" giant hypertrophy of the gastric mucosa and with multiple polyposis—also "localized"—was studied by the author and the findings recorded in some detail. The roentgen findings were misleading, with the localized defect simulating neoplasm of the gastric antrum.

There was marked anemia and achlorhydria; a histamine test was not recorded. At surgery, the proximal stomach was found to be normal and subtotal resection of the Billroth II type was carried out with removal of about 85 per cent of the stomach. A photograph of the surgical specimen shows localized hypertrophy of the gastric mucosa, but true polyposis is inconclusively demonstrated. The postoperative barium roentgenogram which is reproduced seems to show a great deal more than 15 per cent of the stomach remaining.

A review of the literature concerning both giant hypertrophy of the gastric mucosa and multiple polyposis is given.—*Richard E. Kinzer, M.D.*

Ochsner, Seymour Fiske, and Janetos, George P. Benign tumors of the stomach. *J.A.M.A.*, Mar. 15, 1965, *191*, 881–887. (Address: Dr. Ochsner, 1514 Jefferson Highway, New Orleans 21, La.)

The symptoms, histologic varieties and roentgenologic characteristics of 80 cases occurring in the 20 year period prior to 1963 were analyzed. During this same period, 300,000 patients were examined with more than 800 gastric ulcers and 600 gastric cancers diagnosed.

Benign gastric tumors are of many histologic types; in this series adenoma (38) and leiomyoma (26) accounted for 85 per cent with lipomas and vascular tumors next in frequency. Others included were aberrant pancreas, neurogenic tumor, inflammatory polyp, carcinoid, and fibroma with only 1 or 2 of each. There was an approximately equal sex incidence and 47 cases occurred between the ages of 51 and 70 years. The youngest case was 27 and 12 were over 70 years of age. Symptoms were much less common than with malignant lesions. Abdominal pain was present in 41, indigestion in 38, and bleeding in 22. Significant bleeding occurred in 21 per cent of the adenomas and 42 per cent of the leiomyomas.

The lesion was correctly identified as benign in only 14 of the 23 cases which were subjected to gastroscopy.

In 48 patients, positive roentgenographic findings were demonstrated. A sharply defined filling defect was noted in 45, a smooth or only slightly lobulated surface in 44, a round or oval shape in 43, and a submucosal location in 26. Half of these tumors were located in the antrum. Normal surrounding mucosa, peristalsis through the involved portion and flexibility of the gastric wall were also important nonspecific signs of a benign tumor. Special, more specific signs were: (1) multiplicity, usually indicating adenomas and the possibility of Peutz-Jeghers syndrome or neurofibromatosis; (2) pedunculation or prolapse into the duodenum with adenoma; (3) ulceration, most common in leiomyomas and sometimes central necrosis with a "bull's eye pattern"; (4) change in shape with submucosal lipoma; (5) calcification in a leiomyoma; (6) phleboliths in hemangioma; and (7) filiform duct or dimple in aberrant pancreatic tissue.

The differential diagnosis should include bezoars and other foreign bodies, extrinsic pressure defects, postoperative deformity, hypertrophic mucosal folds, hematoma, lymphosarcoma, leiomyosarcoma, primary carcinoma, peptic ulcer, and metastases.

The authors feel that accurate roentgenologic diagnosis of a benign gastric tumor is valuable in the treatment of a relatively poor surgical risk patient in that medical management or limited excision for relief of symptoms is justified.—*A. Raymond Brooker, M.D.*

Rimondi, C. I tumori reticolo- e linfosarcomatosi primitivi dello stomaco. (Primary reticulo- and lympho-sarcomatous tumors of the stomach.) *Ann. radiol. diag.*, 1964, *37*, 204–228. (From: Istituti di Radiologia e del Radio dell'Università di Bologna, Italy.)

Mesenchymal malignant reticulo-hystiocytic tumors of the stomach are not common. They represent 1 per cent of all malignant neoplasms of this organ.

Fairly characteristic roentgenologic signs of this entity are: (1) a contrast between the marked extension of the tumor and the slight rigidity of the stomach which remains movable; (2) thickened but pliable rugae; and (3) ulcerations, occasionally large, presenting clearly defined outlines.

At times the roentgenologic aspect does not differ from that of epithelial carcinoma.

The diagnosis should be suggested by the radiologist but confirmed by the surgeon through biopsy.

This diagnosis implies important consequences from the therapeutic point of view. With opportune radiation therapy, there is the possibility of obtaining long remissions. Of course, other localizations of the neoplasm may appear.—*Anthony A. Blasi, M.D.*

HAN, SANG Y., COLLINS, LOIS C., and PETRANY, ZOLTAN. Emphysematous gastritis. *J.A.M.A.*, June 7, 1965, *192*, 914–916. (From: Departments of Radiology, Baylor University College of Medicine, and Ben Taub General Hospital, Houston, Texas.)

Emphysematous gastritis is produced by an infection in the gastric wall which is due to gas-forming organisms. A case resulting from the ingestion of hydrochloric acid forms the basis of this report. The condition is diagnosed by roentgen examination and is very rare.

The cases reported in the literature have been preceded either by ingestion of corrosive materials, or by gastroduodenal surgery, or by gastrointestinal infarction. There is almost always sudden epigastric pain associated with bloody vomitus. The clinical course is so acute, that it cannot always be differentiated from other acute abdominal conditions, such as perforation of a hollow viscus. Roentgen study is the only definite means, other than exploration, of making a definite diagnosis. Gas in a necrotic gastric wall is evidence of the disease.

The authors' case is the second one reported following ingestion of hydrochloric acid. Denudation of the mucosa of the stomach after ingestion of corrosive materials causes a marked reduction in gastric secretions and the authors believe that this finding is significant since acid secretions normally prevent bacterial growth in the stomach wall.

Excellent reproductions of roentgenograms demonstrate the distention of the stomach and gas bubbles over the entire gastric area both in the supine and erect positions.—*Richard E. Kinzer, M.D.*

DAVEY, W. W., and PEARSON, J. B. Obstruction of the third part of the duodenum. *Brit. J. Surg.*, March, 1965, *52*, 189–193. (From: Department of Surgery, University of Ibadan, Ibadan, Nigeria.)

In Nigeria, duodenal ulcer is common and its most frequent complication is stenosis. In a land where radiologists are rare, it is tempting and sometimes imperative to make the diagnosis on clinical grounds without radiologic confirmation. Sometimes, however, duodenal ulcer is not found.

Five cases are presented in which obstruction was found in the third portion of the duodenum.

There are several reasons why the third portion of the duodenum is liable to obstruction from external pressure: (1) because of the retroperitoneal position, the duodenum is susceptible to pressure against the vertebral column lying behind it; (2) any factor which will narrow the angle formed by the superior mesenteric artery and the aorta or vertebral column will tend to obstruct the duodenum; (3) any expansion of the root of the mesentery will compress the duodenum.

The cases presented consist of: (1) aortomesenteric ileus; (2) inflammatory adhesions secondary to trauma; (3 and 4) tuberculous mesenteric lymphadenopathy; and (5) tuberculous inflammatory stricture of the duodenum.

Other causes which have been reported and are listed by the authors are: (1) obturation from infection; (2) congenital stenosis; (3) atresia or aganglionic segment; (4) intramural hematoma; (5) benign and malignant neoplasm; (6) mid-gut volvulus with bands across the duodenum; (7) duodenal mesocolic band; (8) carcinoma of the pancreas.

The authors conclude that, although the most common cause of duodenal obstruction is ulcer, other causes must be considered, especially tuberculosis. Since obstruction of the third part of the duodenum is a radiologic diagnosis, it is helpful to know this preoperatively, in order to properly modify the technique of management.—*James R. Knapp, M.D.*

YOUKER, JAMES E., and WELIN, SÖLVE. Differentiation of true polypoid tumors of the colon from extraneous material: a new roentgen sign. *Radiology*, April, 1965, *84*, 610–615. (From: Röntgendiagnostik Institute, Malmö Allmänna Sjukhuset, University of Lund, Sweden.)

Polypoid colonic tumors can be divided into three morphologic groups: (a) sessile, (b) intermediate, and (c) pedunculated. Each type has its own characteristic roentgen picture, depending on the appearance of the base of the polyp.

The sessile polyp is flat and difficult to separate from the bowel wall. For this reason it may be confused with infiltrating carcinoma or adherent feces. Careful study of the bowel wall adjacent to such a shadow and repetition of the air contrast barium enema studies are often necessary to establish the true nature of the defect. Villous adenomas, which appear as broad-based sessile growths, can usually be recognized by the fine lacy appearance.

In the intermediate type, a small recess exists between the base of the polyp and the bowel wall. During an air contrast barium enema examination, barium fills the recess between the body of the polyp and the colonic mucosa and also coats the body of the polyp. Hence, two white circles are created on the roentgenograms.

The pedicle of a pedunculated polyp may be identified in profile either by its thin coating of barium surrounded by air, or as a negative shadow in an area of dense barium. The bowel wall may be indented at the point of attachment. The single most reliable roentgen evidence of a pedicle is the "target" sign produced by superimposition of the image of the body of the polyp on the image of the pedicle. This appears as a small circle within a larger barium circle.

The authors reviewed 195 polyps removed from 150 patients by, or under the supervision of, one surgeon. The results showed a high degree of accuracy in predicting the morphologic type. Fifty polyps with the "target" sign all proved to be stalked polyps.

The most common defects which may be confused with polypoid tumors are: fecal material, air bubbles, oil droplets, barium coated diverticula, and mucous strands. Frequently repetition of the barium enema study is necessary to establish the true nature of the defect.—*A. W. Sommer, M.D.*

Wegmann, T., Zollinger, H. U., and Markoff, N. G. Zollinger-Ellison syndrome with terminal hypoglycaemia: report of an atypical case diagnosed in life. *German Med. Monthly*, March, 1965, *10*, 93–98. (From: Department of Medicine, and Institute of Pathology, Kantonsspital of St. Gallen, and Department of Medicine, Kantonsspital of Chur, St. Gallen and Chur, Switzerland.)

The association of gastric hypersecretion, recurrent ulcers of the upper gastrointestinal tract, and pancreatic islet cell tumors, without insulin production, was described as a new syndrome in 1955 by Zollinger and Ellison. The production of large quantities of gastric juice leads to diarrhea in half of the patients. Not typical, however, is the combination of the classic syndrome with hyperinsulinism which was found in 6 of 75 cases.

The authors present a detailed case report of a patient with an islet cell carcinoma of the pancreas and liver metastases, whose death was due to acute terminal hyperinsulinism. Both alpha and beta cells were present in the tumor and the remaining pancreas showed an increase in alpha cells.

Zollinger and McPherson found that tumors of multiple endocrine organs were demonstrated in 21 per cent of the cases of Zollinger-Ellison syndrome. Of the pancreatic tumors in the Zollinger-Ellison syndrome, 50 per cent are carcinoma. Multiple tumors may occur and the malignant tumors have a long natural course with late metastases. Of the 600 islet cell adenomas reported up to 1960, 90 per cent were benign and 10 per cent malignant; 70 per cent of all benign and malignant tumors were solitary growths located in the body or tail of the pancreas.

In the 2.4 per cent of patients in this series who had progressive hypoglycemia, the findings were either pancreatic islet cell adenoma, islet carcinoma, or generalized hyperplasia and hypertrophy of the isles of Langerhans.

Originally, Zollinger and Ellison in describing their syndrome referred only to nonfunctioning islet cell tumors, but there is no doubt that insulin producing tumors may also cause the syndrome.

A summary of the various aspects of the Zollinger-Ellison syndrome is presented together with the description of the possible biochemical basis for each aspect.—*James R. Knapp, M.D.*

Harris, J. D. Rupture of hydatid cysts of the liver into the biliary tracts. *Brit. J. Surg.*, March, 1965, *52*, 210–214. (From: University Department of Surgery, The Queen Elizabeth Hospital, Woodville, South Australia.)

Some degree of intrabiliary rupture is thought to be the commonest of all complications of hepatic hydatid cysts. The presence of a hydatid cyst in the liver results in pressure atrophy on the surrounding parenchyma, vessels, and biliary canals, with resultant leak into a small duct or frank rupture into a large one. The pressure in the cyst is about three times biliary tract pressure, so that following rupture the cyst partially empties itself into the biliary canals until pressure equilibration occurs.

The site of cyst rupture corresponds exactly with that of the localization of the hepatic cyst: 55 per cent into the right canals, 29 per cent left canals, 9 per cent hepatic duct junction, 6 per cent gallbladder, and 1 per cent directly into the common bile duct.

The classic picture will be a young male with a prior history of infestation, presenting with biliary colic and jaundice. Eosinophilia, positive Casoni and hydatid complement fixation tests are strongly in favor of the diagnosis, but an unassailable piece of evidence is the finding of laminated membrane in the feces. In endemic areas, search for this membrane is routine in all cases of biliary colic.

The presence of cholelithiasis does not exclude hydatid disease; in fact hydatid disease leads to the formation of stones, which are said to be found in 10 per cent of cases.

Preoperative cholangiography may be helpful, demonstrating displacement of ducts. Following common duct exploration and clearance of cyst remnants operative cholangiography is imperative to ensure complete clearance of the duct, to locate the mother cyst, and to ascertain the presence or absence of multiple cysts.

Two cases of ruptured hydatid cyst of the liver into the biliary tracts are described, stressing diagnosis, and operative and postoperative complications. Detailed surgical technique is discussed. —*Mark D. Reiss, M.D.*

Zimmon, David S., and Hadgraft, J. W. A new method for hepatolienography. *Radiology*, March, 1965, *84*, 477–482. (From: Departments of Medicine and Pharmacy, Royal Free Hospital, London, England.)

An interesting study from England presents a method for opacification of the liver and spleen using tetraiodophenolphthalein. By this method, rats are given 500 to 1,000 mg./kg. of a microparticulate suspension via the femoral vein. The method of preparation of the microparticulate suspension is described which yields tetraiodophenolphthalein particles ranging from less than 1.0 μ to 5.0 μ in size.

After injection, the rats are roentgenographed immediately and then serially until sacrificed from 1 day to 8 months later. The radiopaque material is deposited in the reticuloendothelial cells of the liver and spleen. Although the solubility of tetraiodophenolphthalein is low, it is gradually released from the reticuloendothelial cells and ultimately excreted from the body. The liver is cleared of contrast material more rapidly than the spleen which may remain faintly opacified for 1 to 4 weeks. Histologic examination of liver, spleen, lung, and kidney; estimation of plasma alkaline phosphatase, aspartate transaminase, bilirubin tolerance tests; and evaluation of weight gain have failed to demonstrate significant toxic effects.

The authors conclude that tetraiodophenolphthalein offers promise and approaches more nearly the ideal criteria than do other agents previously used. The opacification achieved compares very favorably with thorium dioxide. It seems to have little acute toxicity, is easily administered, has a high affinity for the liver and spleen, and is eliminated from the body. However, as the hazards of injecting particulate material are poorly understood, further work is needed before this procedure can be adapted to man.—*Howard R. Stewart, M.D.*

GENITOURINARY SYSTEM

VERHAGEN, ARIE D., HAMILTON, JAMES P., and GENEL, MYRON. Renal vein thrombosis in infants. *Arch. Dis. Childhood*, April, 1965, *40*, 214–217. (From: Surgical Clinic of the Children's Hospital of Philadelphia, Bainbridge Street, Philadelphia 46, Pa.)

Over 300 cases of renal vein thrombosis have been reported. Two thirds of these are in the pediatric age group, and the majority of these are neonates. Though the pathogenesis in infants is obscure, severe gastrointestinal symptoms are often initial or accompanying symptoms.

Two case histories are described. Hematuria, azotemia, and abdominal masses were present in both cases. In one, intravenous urography disclosed an enlarged nonfunctioning kidney on the side of the palpable mass, and exploration was carried out with a preoperative diagnosis of polycystic kidney. Bilateral masses were present in the other case, and inferior vena cavagraphy disclosed obliteration of the lower vena cava with extensive collateral circulation connecting with the azygos system. Nephrectomy was curative in the first case, and vena caval ligation distal to the renal veins, with thrombus suction and extraction performed, in the second case.

In both these surviving patients, thrombosis involved the lower segment of the inferior vena cava. Therefore inferior vena cavagraphy is thought to be a promising method in the study of similar patients, as an addition to routine intravenous urography. Although nephrectomy is favored in strict unilateral renal vein thrombosis with a normal contralateral kidney, restoration of the renal venous return by removal of the thrombus may also be effective.—*Mark D. Reiss, M.D.*

PUIGVERT, A., SOLÉ-BALCELLS, F., and GRAU, J. JURADO. Fundamentos arteriograficos para el tratamiento de la tuberculosis renal. (Arteriographic fundamentals for the treatment of renal tuberculosis.) *Arch. españ. urol.*, Oct.-Dec., 1964, *17*, 269–279. (From: Instituto de Urología, Hospital de la Santa Cruz y San Pablo, Barcelona, Spain.)

The authors have performed 82 arteriographies in renal tuberculosis and have drawn some conclusions as to their value. In the initial stages with erosive lesions around a papilla or the small initial parenchymatous lesions, the intravenous urogram shows positive changes, while the arteriogram may appear to be within normal limits. Larger destructive lesions and stenosing lesions with ectasia of the calyces or renal pelvis show spreading of vessels. Sometimes the amount of functioning tissue of the kidney may be estimated by the blood supply, especially the degree of smaller vessels demonstrated.

It is concluded that the intravenous urogram and the arteriogram complement each other.—*Charles M. Nice, Jr., M.D., Ph.D.*

SKELETAL SYSTEM

MARTIN, P. L., and PLANES, A. Considérations radiologiques sur l'évoluton des fractures articulaires de l'extrémité supérieure du tibia. (Radiologic evaluation of the evolution of articular fractures of the upper end of the tibia.) *J. de radiol., d'électrol. et de méd. nucléaire*, Oct., 1964, *45*, 561–562. (From: Centre de Traumatologie, Bordeaux, France.)

Forty patients presenting fractures of the proximal end of the tibia involving either the external or the medial tuberosity, or both, were studied by the authors by means of routine anteroposterior and lateral roentgenograms, planigrams and arthrograms. Most of the roentgenograms were made in the upright position. In 10 cases, there was 15° valgus, 1 case had marked valgus and 1 showed varus deformity. In 10 cases, in spite of excellent functional results, the authors could note a persistent partial gap at the healed fracture site.

Arthrographic examination in 5 of these 10 cases was performed. In 1 out of the 5, two months after the accident, the contrast medium infiltrated into the gap and even then did not reach the bottom of the gap. This lack of filling of the gap is considered to be due to fibrous tissue filling; as the healing progresses, fibro-cartilagenous tissue is also thought to fill the gap.—*Jirair N. Sarian, M.D.*

SEEDAT, Y. K., and WOLPERT, S. M. Disseminated tuberculosis of bone: report of two cases. *Brit. M. J.*, May 15, 1965, *1*, 1291–1292. (Address: Y. K. Seedat, M.B., Assistant Physician-Lecturer, University of Natal and King Edward VIII Hospital, Durban, Natal.)

Two cases of disseminated tuberculosis of bone in adult Africans are reported because of the rarity of the condition.

Punched-out lesions without sclerosis involving skull, ribs, spine and pelvis were present. Differentiation from multiple myeloma and metastatic malignancy was made by biopsy and by response to specific therapy.—*Henry J. Klos, M.D.*

DELAHAYE, R. P., WEBER, A., LE GOUAS, J. J., and PINET, C. L'ostéopathie fibreuse localisée post-traumatique du tibia: (remaniement pagétoïde localisé post-traumatique de J. A. Lièvre). (Post-traumatic fibrous osteopathy of tibia: [post-traumatic localized pagetoid healing process of J. A. Lièvre].) *J. de radiol., d'électrol. et de méd. nucléaire*, Jan.-Feb., 1965, *46*, 1–10. (From: Services d'Electroradiologie des Hôpitaux militaires d'Instruction du Val-de-Grâce, à Paris, et Dominique-Larrey à Versailles, France.)

Two cases of post-traumatic localized fibrous osteopathy are reported and the clinical, roentgenologic and pathologic findings obtained through the years are discussed.

The first case was observed for 32 years and the second case for 8 years. Because of a history of definite initial trauma, localization to only the traumatized segment of bone, localized clinical signs of pain, hyperthermia and increased vascularity, and periodic progression of the fibrous changes of the bone, the authors are of the opinion that this is not truly a pagetoid osteitis, even though roentgenographically it appears very similar.

Since progressive enlargement of the nutrient vessel canal of the tibia was demonstrated in these cases, the authors believe that vascular disorder is the prime cause of this condition.—*Jirair N. Sarian, M.D.*

AGGARWAL, N. D., and SINGH, HARDAS. Management of fluorotic myelopathy: (preliminary report). *Singapore M. J.*, Dec., 1964, *5*, 208–211. (From: Department of Orthopaedics, Rajendra Hospital, Patiala, and Government Medical College, Patiala, India.)

The skeleton of a patient dying from quadriplegia associated with fluorosis was studied. All the vertebral bodies were larger than normal. Marked ligamentous calcification was associated with large numbers of osteophytes. The spinal canal was narrowed, most markedly at the lower end of the third cervical vertebra.

This apparent etiologic relationship between fluorotic myelopathy and cord compression led to extensive cervical laminectomies in 2 advanced cases of the disease. Both patients were males in their forties, living in endemic areas for fluorosis, having progressive weakness for several years in all 4 extremities, and quadriplegia for 6 months. Urine, blood, and bone fluoride levels were elevated. Roentgenographic examination showed increased density of all bones, with osteophytosis and ligamentous calcification.

The results were better than expected following cervical laminectomy, and both patients gradually recovered function in all 4 limbs. Extensive extirpation of the numerous osteophytes narrowing the canal were not attempted, but simple laminectomy for cord decompression was so beneficial as to be suggested in cases of fluorotic myelopathy.—*Mark D. Reiss, M.D.*

CANIGGIA, A., GUIDERI, R., and FORCONI, S. The diagnostic value of needle biopsy of bone. *Panminerva med.*, Jan.-Feb., 1965, *7*, 15–29. (Address: Prof. A. Caniggia, Ist. Semeiotica Medica, Policlinico, Siena, Italy.)

The authors give a brief historic outline of various techniques of biopsy investigation of the skeleton. The trocar of Mazabraud and the technique of bone tissue removal are thoroughly described with many microscopic sections in color accompanying the article. The advantages and usefulness of biopsy investigation of the skeleton are given.

The trocar itself is a small steel tube with a circular and saw-toothed end. The centers most preferred for bone biopsy are the iliac crest and the greater trochanter. However, any site where investigation is desired may be used.

The article contains descriptions of different tissues which may be encountered on a histologic level. These include: (1) needle biopsy of bone for evaluation of bone mass; (2) needle biopsy of bone for evaluation of osteoblastic or osteoclastic activity; (3) biopsy of bone in the evaluation of osteoid osteoma; (4) needle biopsy of bone for evaluation of elementary calcified structures of the bone tissue; (5) needle biopsy for evaluation of medullary changes; (6) biopsy for the documentation of tumor metastasis.—*David C. Alftine, M.D.*

BLOOD AND LYMPH SYSTEM

NORDENSTRÖM, BJÖRN, and GRIM, STIG. A method for determination of blood flow with use of roentgen contrast medium. *Radiology*, April, 1965, *84*, 644–655. (From: Department of Roentgenology, Thoraxkliniken Karolinska Sjukhuset, and Development Section, Elema-Schönander AB, Stockholm, Sweden.)

The pumping capacity of the heart is in a high degree dependent upon the effectiveness of the valves. There is still, however, no practical method by which reliable quantitative data concerning this function can be obtained, although important contributions toward the solution of this problem have been made from several quarters.

The present work is a preliminary report on a method for simultaneously measuring the effective blood flow on the basis of the dilution of injected roentgen contrast medium and the roentgenologic measurement of stroke volume and pulse frequency. The stroke volume is calculated by measuring the volume variations of the left ventricle on serial roentgenograms exposed in two projections at right angles to each other during the passage through the ventricle of the contrast fluid injected.

In the new densitometric instrument, a roentgen beam is used instead of light. The transmission of the roentgen beam is measured with a photo-cell through a fluorescent screen.

The contrast medium is injected via a heart catheter in the pulmonary artery from a Gidlund injection syringe. Serial exposures of the passage of the contrast medium through the left ventricle make it possible to calculate stroke volume and, with known heart frequency, the volume work of the left ventricle. During passage of the bolus of contrast medium in the aorta, continuous sampling of the blood is undertaken via a catheter by means of a motor-driven suction syringe. This sampling is made with the aid of the densitometric unit. The roentgen tube in this unit is connected with a small roentgen apparatus, which in turn is fed through the current stabilizer. The signals from the densitometric unit are amplified and finally recorded by a direct writing instrument.

The technique is well illustrated, and the formulas for calculation are presented. It omits several sources of error connected with conventional dilution methods, and reportedly has given extremely stable and reproducible measuring values in both calibrations.—*Paul M. Kroening, M.D.*

ADAMS, DOUGLASS F., OLIN, TORD B., and KOSEK, JON. Cotton fiber embolization during angiography: a clinical and experimental study. *Radiology*, April, 1965, *84*, 678–681. (From: Department of Radiology, Stanford University School of Medicine, Palo Alto, Calif.)

This brief article reports 4 cases of cotton-fiber embolization following selective arteriography and describes a controlled experimental evaluation of this phenomenon in laboratory animals.

Three of the 4 clinical cases occurred during selective renal arteriography and 1 during percutaneous carotid arteriography. The renal studies were accomplished by femoral catheterization utilizing the Seldinger percutaneous technique. Each of these cases proved to be hypernephroma and the fourth case an inoperable Grade III astrocytoma. The pathologic examination also revealed evidence of arteriolar emboli and infarction in each kidney specimen and arteriolar embolus without infarction in the astrocytoma biopsy. The multiple renal infarctions were cortical in location, small in size, and contained strongly birefringent, semi-crystalline fibers, of variable width and length, usually about 8×50 micra. Combinations of these intraluminal fibers with endothelial cell proliferation and hypertrophy were found to be reproducible factors that may result in tissue infarction. These fibers were found to be identical to cotton fibers from surgical sponges and their source apparently had been from the container of heparinized saline used for guide wire cleaning and catheter irrigation.

The experimental method employed to investigate this problem was to collect and concentrate 800 cc. of heparinized saline solution from the angiography table after completion of routine angiographic procedures and selectively catheterize the renal artery of the laboratory animal (dogs and rabbits). The opposite renal artery was simultaneously injected with an equal quantity (5 cc.) of sterile saline taken directly from the unopened commercial preparation. One week later the animal was sacrificed and each kidney examined. In each case multiple fiber emboli and infarctions were demonstrated in the kidney into which the cotton fiber preparation had been injected and the opposite kidney was in each case found to be normal both grossly and microscopically.

If pregnancy or lactation were not associated with the breast cancer, younger patients did about as well as older patients.

The site of the primary lesion in the breast substance made little difference in survival. Histologic grade was recorded in 549 cases. Grades 1 and 2 had higher survival rates (CSR 68.9 per cent and 51.2 per cent) than Grade 4 (CSR 40.0 per cent).

For 145 untreated patients in the review group, the CSR was 9.7 per cent 5 years after clinic registration and 35.2 per cent 5 years after the first recorded symptom. Corresponding rates for the whole review series were 45.3 per cent and 52.3 per cent, respectively. As expected, the untreated group patients were older, had delayed longer before registration and had more advanced disease.

For all extent groups combined, the highest crude survival rates were observed after radical mastectomy alone, or simple or radical mastectomy combined with radiotherapy. Survival rates were lower with simple mastectomy or local excision alone.

Great caution is urged in assessing the treatment results due to lack of completeness of some records and the variable techniques used in treatment.—*Newell K. Richardson, M.D.*

Crile, George, Jr. Rationale of simple mastectomy without radiation for clinical Stage 1 cancer of the breast. *Surg., Gynec. & Obst.*, May, 1965, *120*, 975–982. (From: Department of General Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio.)

There is evidence that some human cancers are antigenically different from their hosts and evoke an immunologic response. Theoretic, laboratory and clinical evidence makes it necessary to re-evaluate the principle of prophylactic lymph node dissections for breast cancer.

One hundred and thirty-five operable breast cancer patients seen at the Cleveland Clinic between 1955 and 1957 have been evaluated. Seven to 8 years after treatment the survival of patients with Stage 1 cancers of the breast was a little higher after simple than after radical or modified radical mastectomies. The survival of patients with previously untreated and operable breast cancer was higher in the years in which the fewest radical operations and the least irradiation was used.

Stage 1 cancer patients treated with simple mastectomy in whom axillary metastasis occurred were treated by delayed axillary dissections. The 5 to 8 year survival rate and survival rate free of disease are as high as in Stage 1 patients treated by radical mastectomy and who had proven lymph node metastasis.

In mice on whose feet homologous tumor S180 had been implanted, removal of the regional lymph nodes eliminated much of the host immunity to subsequent implants of S180. Irradiation of the regional lymph nodes had a similar effect.

Radical resection of the regional lymph nodes and an implanted isologous tumor, sarcoma 1, in strain A mice, resulted in greater spread to distant lymph nodes than did simple removal of the tumor.

A large randomized study of the results of simple *versus* radical treatment of Stage 1 breast cancer is urged by the author.—*John T. Underberg, M.D.*

Harrison, Edgar G., Jr., and Witten, David M. Occult or unsuspected breast carcinoma. *GP*, May, 1965, *31*, 78–88. (From: Section of Surgical Pathology, and Section of Roentgenology, Mayo Clinic and Mayo Foundation, Rochester, Minn.)

Early carcinoma of the breast may go unsuspected because of its occult nature or because the overt signs go unrecognized clinically. Increased awareness of the clinicopathologic conditions, mammography and early biopsy should improve the management of breast cancer.

Paget's disease of the nipple is an intraepithelial adenocarcinoma associated with an underlying ductal carcinoma. Paget's disease occurs in 3 per cent of mammary carcinomas and 20 per cent of comedocarcinomas are associated with Paget's disease. It rarely occurs in men. Nipple erosion, if persistent, should be biopsied. Radical mastectomy is the treatment of choice. A benign condition, florid papillomatosis of usually the lactiferous ducts, may be associated with nipple erosion and enlargement and must be differentiated clinically and pathologically.

Nipple discharge, particularly if blood tinged or occurring in an older woman, should be viewed with concern. Even when bloody, however, the usual etiology is a benign condition such as intraductal papilloma, ductal ectasia, or periductal mastitis.

About 1 per cent of breast carcinomas occur bilaterally simultaneously. Whenever one breast has been removed for carcinoma, the remaining breast should be periodically examined clinically and by mammography. In comedocarcinoma, which constitutes about 10 per cent of mammary carcinomas, a bilateral incidence of 8 per cent has been reported. The rare *in situ* lobular carcinoma was reported to occur bilaterally in 23 per cent of 26 cases; in the male breast bilateral lesions occurred in 2.7 per cent of cases. The 5 year survival rates are far from hopeless in those cases where both breasts become involved.

Intracystic carcinoma is rare but mammary carcinoma may be hidden by benign diseases, especially fibrocystic disease. Fibrocystic disease may also hide a carcinoma on mammography. The incidence of eventual breast cancer is greater in patients treated clinically for fibrocystic disease.

Metastatic lesions, especially of the axillary lymph nodes, may be the first indication of an occult carcinoma. The survival rates for occult carcinoma with axillary metastasis treated by radical mastectomy have been reported as better than in ordinary axillary metastatic breast cancer. Rarely carcinoma may also arise in aberrant breast tissue.

Circumscribed breast masses are more often looked upon as benign. Medullary adenocarcinoma with lymphoid stroma is usually large, bulky and circumscribed. Mucous or colloid carcinoma is circumscribed and expansile. Adenoid cystic carcinoma or cylindroma may be circumscribed or lobulated.

Inflammatory carcinoma may be mistaken for mastitis, particularly in pregnancy or lactation, and delay in treatment may result. Bilateral extension of the breast swelling is seen in about one-third of the cases.

Carcinoma of the male breast occurs in about 1 per cent of breast carcinoma.

Mammography is an aid in the earlier detection of breast cancer. Carcinoma is usually irregular or spiculated and 29 per cent of one series of cases had granular calcifications visible roentgenographically.

All discrete masses or questionable breast conditions, no matter how benign they seem, must be considered malignant until proven otherwise.—*John T. Underberg, M.D.*

Brady, L. W., Faust, D. S., Johnson, C. R., and Wolferth, C. C., Jr. Carcinoma of the esophagus: therapeutic results using supervoltage techniques. *Radiol. clin. et biol.*, 1965, *34*, 17–31. (From: Departments of Radiology and Surgery, Hahnemann Medical College, Philadelphia, Pa.)

Carcinoma of the esophagus remains one of the most distressing diseases facing the surgeon or radiation therapist. The prognosis is poor in all cases, with untreated patients surviving less than 6 months. Treatment has not altered this grave picture significantly.

The authors report their results, using supervoltage techniques. A total of 53 patients were treated—27 definitively and 26 palliatively—with 2 mev. Van de Graaff generator in such a manner as to include the entire esophagus without harm to the surrounding tissues. Using 1 anterior and 2 oblique posterior ports, 6,000 rads were delivered to the tumor in 7 weeks for definitive therapy. For palliation only, using the same ports, 3,000 rads were delivered to the tumor in 3½ weeks.

Only 16 patients survived after 1 year, 1 after 2 years and none after 3 years in the definitive therapy group. Only 2 patients survived 1 year in the palliation series.

However, preoperative irradiation merits further investigation. In 5 such cases, local tumor control was obtained in 4. Two had no evidence of local or metastatic disease at the time of their death.—*W. J. Carmoney, Jr., M.D.*

Jacobs, M. L., and Marasso, F. J. A four-year experience with total-body irradiation. *Radiology*, March, 1965, *84*, 452–456. (From: Department of Radiation Therapy, City of Hope Medical Center, Durarte, Calif.)

In 1960, the City of Hope Medical Center acquired an especially designed multiple roentgen source chamber to deliver whole-body irradiation. One of the prime uses for this chamber was an attempt to ablate body immune mechanisms and relate this phenomenon to homologous tissue grafting. During the course of this study, drugs replaced radiation for these purposes. The total body irradiation was continued, however, in the hope that some palliation might be achieved in leukemia and disseminated cancer when other modalities had failed or could not be employed. Fifty-two patients have received treatment and the results are presented.

It is concluded that total-body irradiation has some usefulness, but it is limited. It is suggested that a more complete evaluation is indicated, and the study will be continued. No evidence has accumulated to suggest any definite advantages of the special multiple source, total-body irradiation chamber over the readily available single source, conventional radiation equipment which could be used by any radiotherapist interested in this problem.—*Paul M. Kroening, M.D.*

Moretti, S., and Rimondi, C. L'importanza dell'angiopneumografia nella diagnosi differenziale fra recidiva tumorale e sclerosi nei neoplastici polmonari curati con alte energie. (The importance of pneumo-angiography in the differential diagnosis between tumor recurrence and sclerosis in pulmonary neoplasms treated with high energies.) *Radiobiol., radioter. e fisica med.*, Nov.-Dec., 1964, *19*, 451–480. (From: Istituti di Radiologia e del Radio dell'Università di Bologna, Italy.)

Alterations of pulmonary artery branches are observed in over 50 per cent of patients affected by pulmonary neoplasm. They are represented by displacements at the vessels, pressure defects, rigidity of the wall, intrinsic filling defects and even by occlusion.

In the last two years the authors have subjected 12 patients previously irradiated with high energies for pulmonary neoplasm, to pneumo-angiographic examination at intervals of 6 months and 2 years.

Conventional roentgenography demonstrated changes which were characteristically radiofibrotic, *i.e.*, dense band-like radiating opacities, well defined rectilinear densities limited to the field of radiation.

Changes diagnostic of neoplastic recurrence were also observed, *i.e.*, rounded densities with a tendency toward extension superimposed on the radiofibrotic changes.

The authors have sought to establish angiographic criteria for the differentiation of postradiation fibrosis and tumor recurrence. They conclude that characteristic postradiation, pleuro-pulmonary angiographic alterations are difficult to determine. In the interpretation of the vessel changes one must consider clinical data and conventional roentgenography.—*Anthony A. Blasi, M.D.*

BELOTTE, J., GARY-BOBO, J., POURQUIER, H., and PAGES, A. Contribution à l'étude des sténoses digestives profondes postradiothérapiques: à propos des 5 observations. (Contribution to the study of marked post-radiotherapeutic stenoses of the digestive tract; on the basis of 5 observations.) *Presse méd.*, March, 1965, *73*, 851–856. (From: Chaire de Carcinologie et Centre Régional de Lutte contre le Cancer, Pavillon Curie, Clinique Saint-Eloi, 34-Montpellier, France.)

The authors report 4 cases of stenotic changes of the sigmoid and rectosigmoid regions and 1 case of stenosis of the upper part of stomach demonstrated after deep radiotherapy.

Only in 1 case was there a histopathologic proof of postirradiation fibrotic stenosis of the sigmoid, yet in the other cases the roentgen findings were quite suggestive of similar change.

In all cases, the radiation dose exceeded the maximum limit and symptoms and signs of stenosis appeared 6 months or more after deep radiotherapy.—*Jirair N. Sarian, M.D.*

MARKSON, J. L., and FLATMAN, G. E. Myxoedema after deep x-ray therapy to the neck. *Brit. M. J.*, May 8, 1965, *1*, 1228–1230. (From: Western Infirmary and Stobhill General Hospital, Glasgow, Scotland.)

Five cases of myxedema following external irradiation of the neck have been encountered by the authors in the past few years.

In each case malignancy other than that of the thyroid gland was the indication for radiotherapy. Doses to the thyroid gland of from 2,600 to 4,850 rads resulted in myxedema in from 3 to 36 months. The doses were less than those necessary to ablate normal thyroid gland.

Thyroid auto-antibodies in low titer were found in each case and the authors suggest that irradiation of the thyroid gland may have initiated an auto-immune reaction which, in turn, may have ablated the gland.—*Henry J. Klos, M.D.*

RADIOISOTOPES

BULL, JAMES W. D., and MARRYAT, JOHN. Isotope encephalography: experience with 100 cases. *Brit. M. J.*, Feb. 20, 1965, *1*, 474–480. (From: Institute of Neurology, Queen Square, London, England.)

Isotope encephalography has earned its place in the neurologic diagnostic armamentarium by virtue of ease of performance, lack of morbidity, and because of high diagnostic accuracy. In a review of 100 consecutive patients over the age of 18, referred because of clinically suspected intracranial masses, the authors document the last point. The patients were given 1 ml. meralluride intramuscularly 24 hours prior to scanning in an attempt to reduce the dose to the kidneys estimated at 50–60 rads. (This may or may not be efficacious.) Scans were performed using Hg^{203} chlormerodrin administered intravenously in a dosage of 10 μc/kg. up to a maximum of 700 μc and scanning with a Picker Magnascanner 5 hours later. Scans were first done on the clinically suspect side and then the appropriate frontal plane scan, either prone or supine, was performed on the basis of the lateral scan. Later in this series, the photo scan was performed using a film with a latent image of the skull. This was previously exposed using essentially the same geometry as during scanning. The double exposure allowed easy accurate localization.

There were 50 positive cases, none of which was false; 44 negative cases, of which 15 were falsely negative and 4 of which may have been falsely negative. Of the 6 scans thought equivocal, 3 were found to have lesions at surgery, 2 are being followed, and 1 developed a positive scan 7 months later. Because of possible kidney dosage, scans were not repeated with Hg^{203}. Lack of complete surgical and necropsy proof precludes precise analysis, but in most cases, overwhelming clinical and radiographic evidence was supportive. Of the positives, there were 22 astrocytomas, 11 metastatic lesions, and 9 miscellaneous lesions, including hematoma, aneurysm, and abscess. Occasionally, the scan picked up lesions missed by angiography and air contrast study, although the converse was more often true. The appearance of the scan could be helpful in making the histologic diagnosis by keeping in mind the normal anatomic relations of the falx and the corpus callosum. Astrocytomas involving the corpus callosum give a pathognomonic "butterfly" appearance in the frontal view with bifrontal masses connected by an isthmus. Meningioma is a likely diagnosis when a frontal pole mass crosses midline. Multiple masses nearly always indicate metastases, although meningiomas may be multiple.

Lack of understanding of the process of tumor localization makes understanding of all false negatives unlikely. Pituitary tumors and well differentiated astrocytomas seldom give positive scans. A tumor less than 2 cm. in diameter is probably beneath resolution. A focus depth of 6.5 cm. of the scanning collimator means that deeply situated lesions may be missed. Development of more sensitive detector methods and use of shorter half-life isotopes with more suitable gamma emission may remedy some of these difficulties and make an already proven method even more useful.—*Fredrick S. Mishkin, M.D.*

Sodee, D. Bruce, Renner, Robert R., and Di Stefano, Berardino. Photoscanning localization of tumor, utilizing chlormerodrin mercury 197. *Radiology*, May, 1965, *84*, 873–876. (From: Department of Nuclear Medicine, Renner Clinic Foundation and Doctors Hospital, Cleveland Heights, Ohio.)

The authors present their preliminary clinical work describing the accumulation of Hg^{197} neohydrin in tissue that had undergone carcinomatous change. During their investigation with this radioisotope as a brain-scanning and renal-scanning substance it was found to have a measurable accumulation in all areas of the body that contained carcinoma except those organs which normally concentrate mercury to a high degree (liver and kidney). This accumulation was best demonstrated on the 24 hour post-dose scan as the blood background at 24 hours had been reduced to a minimum and was readily demonstrated by *in vivo* counting techniques and by their clinical photo-scanning techniques. A 3×2 inch sodium iodide crystal was used initially in this study but during the last portion of the study a 5×2 inch crystal was substituted.

The authors hope that this preliminary clinical study will promote interest in the biochemical reasons behind such accumulation and anticipate that this simple scanning technique will have widespread application in the detection of cancer. They feel that, with precise delineation of the carcinomatous area, radiation therapy fields can be more accurately planned and the therapeutic results better determined.

Their methodology is described and 2 case reports are presented.—*Donald N. Dysart, M.D.*

Gottschalk, Alexander, and Anger, Hal O. Renal scintiphotography with the gamma-ray scintillation camera and Hg^{203}-neohydrin. *Radiology*, May, 1965, *84*, 861–867. (From: Donner Laboratory of Medical Physics and Biophysics, University of California, Berkeley, Calif.)

Renal scanning is a valuable clinical procedure which is particularly useful for (a) detecting masses in the kidneys, (b) identifying the degree of parenchymal function, (c) localizing the kidneys prior to biopsy and (d) demonstrating unilateral vascular or other segmental disease.

In spite of the recognized worth of this procedure, conventional scintiscanning requires at least 45 minutes for the examination and the usual dose of Hg^{203} neohydrin is 100 to 150 μc which produces renal irradiation estimated to range from about 8 to 20 rads. However, with the newly developed scintillation camera, the examination time can be reduced by a factor of 10, with the additional advantage of reducing the amount of renal irradiation, and the rapid performance of study in the oblique views without unduly prolonging the examination time.

The authors present a brief description of the scintillation camera along with the features of its use. Basically, the unit consists of a multiple parallel hole collimator which projects a gamma ray image onto a large single sodium iodide crystal ($11\frac{1}{2}$ inches in diam. $\times \frac{1}{2}$ inch). The light produced is detected by a bank of 19 photo-multiplier tubes which view overlapping areas of the crystal. By appropriate circuits, the scintillations are displayed on an oscilloscopic screen, oriented correctly on the X and Y axis. The resultant image is readily recorded photographically and the pictures obtained are called "scintiphotographs."

The sensitivity of the gamma ray scintillation camera allows excellent scintiphotos with only 3 to 5 minute exposure times with a scanning dose of 100 μc of Hg^{203} neohydrin. Comparable results can be obtained with 5 to 10 minute exposures with only a 50 μc dose and good studies can be achieved with a dose as small as 5 μc in the pediatric patient which gives a renal dose of less than 1 rad. Several interesting scintiphotos are presented which demonstrate the usefulness of the instrument including the anterior and oblique scans which are easily obtained. The authors feel that these views will extend the scope and diagnostic accuracy of renal scanning.—*Edward B. Best, M.D.*

Croll, Millard N., Brady, Luther W., Brodsky, Isadore, and Stanton, Leonard. A new agent for splenic scanning: BMHP. *Radiology*, March, 1965, *84*, 492–495. (From: Departments of Radiology and Medicine, The Hahnemann Medical College, Philadelphia, Pa.)

BMHP, or bromo-1-mercuri-2-hydroxypropane, was first synthesized as a result of work done by Wagner in expounding upon a discovery by Kessler, Lozano, and Pitts, in 1957, that 1-iodo-mercuri-2-hydroxypropane concentrated in the spleen of dogs after intravenous injection. This report of 15 studies utilizing Hg^{197} BMHP, Hg^{203} BMHP, and Hg^{197} MHP, offers supportive data to Wagner's series of 110 cases, reported in 1964.

Following venipuncture, 100 μc of Hg^{203} BMHP was mixed in the syringe with the patient's blood in a concentration of 1 mg. of mercury per 2 ml. of whole blood. This was immediately re-injected and serial blood samples were taken at 30 minute intervals for the first 3 hours and then hourly for 6 hours. Total urine and stool collections were done for 4 days. Integral counting over the spleen, liver, kidneys and sacrum was performed at varying time intervals for 3 days. The abdomen was scanned 2 hours after administration of the radioisotope. Chromatographic urine studies were performed and the patient's blood count and blood volume determined.

The BMHP-labeled erythrocytes cleared the circulation with a half-time of 20 to 100 minutes. The peak level of radioactivity over the spleen occurred 1 to 4 hours after administration, and clearance from the spleen was almost complete in 6 hours. The radioactivity then appeared in the liver and kidneys, with 25 per cent in the liver and 75 per cent in the kidneys. The liver activity was excreted in the stools in 4–6 days. The radiomercury in the kidneys was excreted in the urine at a rate of 0.3–0.5 per cent per day. External counting revealed no evidence of localization in the bone marrow, and the chromatographic examination identified the presence of Hg^{203} mercuhydrin in the urine.

Calculation of radiation dosage to the kidneys using Hg^{203} (Quimby-Marinelli formula) yielded 76 rads to each kidney. Therefore, it was decided to use Hg^{197} which gave comparable scan results and only 3.6 rads to each kidney.

The authors' most recent studies have been performed with Hg^{197} MHP since it is technically easier to prepare and yields equally good splenic scans.—*Howard R. Stewart, M.D.*

Smart, J. Gordon. The use of P^{32} in the treatment of severe pain from bone metastases of carcinoma of the prostate. *Brit. J. Urol.*, April, 1965, *37*, 139–147. (Address: Senior Surgical Registrar, St. Thomas' Hospital, London, England.)

The correlation betweeen radiologic bone changes and pain from metastasis is variable. However, evidently severe pain tends to occur and cause a problem in the management of metastatic carcinoma of the prostate.

The author treated 9 cases of metastatic carcinoma of the prostate utilizing intravenous radioactive P^{32} and testosterone. It is well known that P^{32} is taken up in greater quantities in neoplastic tissue. With male hormone administration, this uptake is increased 15 to 20 times.

The following method was used by the author. If patient had been on stilbestrol therapy, this drug was discontinued at least for one week prior to P^{32} therapy. During the middle 7 days of 17 daily intramuscular injections of 100 mg. of testosterone propionate, intravenous P^{32} was given. Seven daily doses of 1.43 ml. from the original 10 ml. containing 10 mc activity was administered. This totaled 8.68 mc dosage over the 7 days. Estrogen therapy was reinstituted 1 week after the last testosterone injection.

The treatment resulted in disappearance of pain in 4 patients, moderate relief in 2 patients, mild relief in 1 patient, and the remaining 2 patients terminally had an increase in pain.

Transient hematopoietic depression occurred. Therefore, it is necessary to follow the blood picture closely in these patients.—*W. J. Carmoney, Jr., M.D.*

Leger, L., Justin-Besançon, L., Farel, H., Baillet, J., and Patel, J.-Cl. La splénoportographie isotopique: étude critique de la mesure du débit hépatique par une technique de courbe de dilution isotopique. (Isotopic spleno-portography; critical study of the measure of hepatic flow by means of a technique of isotopic dilution curve.) *Presse méd.*, Feb., 1965, *73*, 391–396. (From: Services du Pr. Justin-Besançon [Hôpital Broussais], et du Pr. Leger [Hôpital Cochin], Paris, France.)

The authors review the various methods and techniques which have been used by other workers in determining hepatic blood flow and then describe their own technique and findings in 27 patients. This procedure is considered particularly significant in hepatic cirrhosis. A splenic puncture is performed following local anesthesia and roentgenoscopic localization of the cardiophrenic angle. The splenic pressure is manometrically determined.

The authors then inject 50 μc of radioactive I^{131} tagged human serum albumin through the spleen and by placing a scintillation probe over the region of the liver an isotope dilution curve is obtained.

Striking findings were observed in cases of cirrhosis of the liver, where the peak of a high curve is rapidly obtained following the injection into the spleen. However, after a protocaval shunt the curve rises slowly and levels off rapidly into a plateau. The time elapsed between the intrasplenic injection and the peak of the curve is 17 seconds in cases of cirrhosis, but following a portocaval shunt the peak of the curve, which is very low, is reached in 54 seconds after the injection. This examination is simple and easy to perform and the results are promptly obtained. The procedure dispenses with formerly used and more cumbersome absorption and excretion studies of substances metabolized by the liver.

Six figures, including reproductions of two splenoportograms, dilution curves and one table accompany this interesting article.—*William H. Shehadi, M.D.*

Ellis, Frank, Parker, Joan R., Bulbrook, R. D., and Deshpande, N. The uptake of radioactivity by normal and neoplastic human breast tissues after administration of tritiated testosterone. *Brit. J. Surg.*, Jan., 1965, *52*, 54–58. (From: Department of Surgery, Guy's Hospital Medical School, and Division of Chemistry and Biochemistry, Imperial Cancer Research Fund, London, England.)

Recent evidence suggests that the biologic characteristics of some breast tumors may be correlated with the hormonal environment in which they grow. For example, it has been shown that patients who excrete less urinary androgen metabolites than they do 17 hydroxycorticosteroids have a more rapid recurrence of the tumor after mastectomy and generally fail to respond to subsequent adrenalectomy or hypophysectomy.

The authors felt that further information in this regard might be gained by investigating the androgen content of normal and neoplastic breast tissue.

This paper reports on the accumulation of tritium tagged testosterone in normal and neoplastic breast tissue after its intravenous administration in 34 patients about to undergo radical mastectomy. A dose of 5 to 8 μc in 15 ml. of saline was injected between 10 to 45 minutes prior to surgery. The surgical specimens were subjected to both histologic examination and estimation of their radioactive content. The cellular uptake of the radioactivity was calculated by dividing the cells counted per unit area into the c.p.m. per gram wet weight of the tissue. The plasma content of the tissue was also determined by preoperative estimation of the plasma volume using RISA. The last measurement considered consisted of an estimation of the extracellular fluid volume. This was accomplished by determining the distribution of Br^{82} in samples of the tissue removed at surgery. The Br^{82} was injected intravenously 4 hours prior to the operation.

The results of the study confirm that both normal breast tissue and tumor tissue accumulate more radioactivity than fat or muscle on a wet weight basis. Initially, more radioactivity is taken up by unit weight of the tumor than by normal breast tissue; and this activity is lost at a faster rate. Neither tissue retains radioactivity; they lose it exponentially in the same way as muscle or fat. If the differences in cellularity between normal breast tissue and tumor are taken into account, the finding that tumor may accumulate radioactivity to a slightly greater degree is reversed. As yet, it is not known whether testosterone is accumulated within the cell. If it is, the findings would indicate that as the cell becomes neoplastic, it loses its ability to accumulate testosterone. It would also be interesting to see whether the clinical results of subsequent treatment of recurrences with testosterone bore any relationship to the ability of the primary tumor to concentrate the hormone.

Four graphs and 3 charts accompany this paper.—*Kenneth M. Nowicki, M.D.*

CHEMOTHERAPY

Ezdinli, Ediz Z., and Stutzman, Leon. Chlorambucil therapy for lymphomas and chronic lymphocytic leukemia. *J.A.M.A.*, Feb. 8, 1965, *191*, 444–450. (Address: Dr. Ezdinli, 666 Elm Street, Buffalo, N. Y. 14203.)

Chlorambucil (leukeran), an oral alkylating agent and water soluble aromatic nitrogen mustard derivative, has long been known to be effective in the treatment of chronic lymphocytic leukemia.

The authors administered 205 courses of chlorambucil to 126 patients with lymphoma or chronic lymphocytic leukemia from 1955 to 1963. In evaluation, they demonstrated a 77 per cent worthwhile response in 43 patients with Hodgkin's disease; of 51 patients with chronic lymphocytic leukemia, more than 50 per cent showed improvement; and of 20 patients with lymphosarcoma, more than 50 per cent obtained a favorable response, while only 1 out of 12 patients with reticulum cell sarcoma derived benefit.

The general mode of therapy consisted of daily oral doses of chlorambucil in the range of 6–12 mg., over a period of 4–8 weeks. Weekly evaluations of blood cell counts and dosage schedules were carried out. Therapy was continued until there was a result or until hematologic toxicity appeared. The only important sign of toxicity was considered to be bone marrow depression; this generally had a gradual rather than a precipitous onset.

Subsequent retrials with chlorambucil showed beneficial responses only when the initial trial produced a definite response. Combined therapy of chlorambucil and cortisone in a small number of patients with anemia and thrombocytopenia along with leukemia allowed full dose administration, but did not enhance the therapeutic effectiveness.

The median survival times in this study were: Hodgkin's disease (43 cases) 5.3 years; chronic lymphatic leukemia (51 cases) 5.2 years; lymphocytic lymphosarcoma (20 cases) 4.1 years; and reticulum cell sarcoma (12 cases) 4.1 years. All patients had systemic disease not likely to be controlled by local radiation therapy.

In comparing the response of chlorambucil to radiation therapy effect, it was shown that of 97 patients chlorambucil produced good response in 60 per cent, while the local response with radiation therapy was 90 per cent. A considerable degree of sensitivity to radiation was retained after chemotherapy with chlorambucil. There was an apparent relationship between failure to respond to chlorambucil therapy and short duration of the disease prior to treatment. In the drug failure group, the disease had been present for an average of 18 months, while the duration of the disease in those patients who showed a strong response was 35 months.

The response of lung lesions to chlorambucil therapy in 50 per cent of the patients is considered important since therapy of this region is hazardous. A trial of chemotherapy with agents such as chlorambucil seems warranted prior to the institution of radiation therapy with portals covering peripheral lung tissue.

The response to chlorambucil therapy also has prognostic significance because those patients who responded to therapy had considerably better survival rates than those unresponsive to the drug.

The response rate of the leukemia cases in this series is among the lowest of the several series reported in the literature. Reticulum cell sarcoma was very resistent, and Hodgkin's disease showed a higher response rate than in most series reported in the literature.—*Ronald Schaupp, M.D.*

Brown, John H., and Kennedy, B. J. Mithramycin in the treatment of disseminated testicular neoplasms. *New England J. Med.*, Jan. 21, 1965, *272*, 111–118. (From: Department of Internal Medicine, University of Minnesota Medical Center, Minneapolis, Minn.)

Disseminated testicular neoplasms, other than seminoma, have not been effectively controlled by radiation therapy or by chemotherapeutic agents.

The authors report the utilization of mithramycin, an antibiotic prepared from an *Actinomyces* culture belonging to the genus *Streptomyces*, in the treatment of 12 patients with disseminated germinal neoplasms of the testis.

A review of the literature shows that an objective remission was obtained in 12 of 24 patients with embryonal cell carcinoma of the testis treated with mithramycin. Of 10 patients with other types of testicular neoplasms only transient regressions have been reported in 3.

In the authors' series, objective regressions of tumor occurred in 7 of the 12 patients with disseminated germinal neoplasms of the testis treated, the responses being primarily in embryonal cell carcinoma. The regressions noted consisted of a shrinkage of 50 per cent or more of the measured tumor masses or of disappearance of the lesions.

The manifestations of mithramycin toxicity in the authors' study consisted of gastrointestinal reactions, dermatologic changes, hepatocellular damage, renal toxicity, thrombocytopenia and electrolyte disturbances. Increased toxicity occurred in patients who had received radiation therapy as a part of the initial treatment of the primary tumor.

The toxic manifestations of this new chemotherapeutic agent, mithramycin, do not preclude its practical application in cancer therapy and in the authors' opinion, the drug demonstrates a specificity for embryonal cell carcinoma.—*Luther W. Brady, M.D.*

Wagner, Donald E., and Baum, Stanley. Preliminary arteriography in hepatic artery infusions for cancer. *Surg., Gynec. & Obst.*, April, 1965, *120*, 817–819. (From: Departments of Surgery and Radiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pa.)

The authors advocate preliminary hepatic artery angiography in patients who are candidates for chemotherapeutic infusion of the hepatic artery in malignancy. They use the Seldinger femoral puncture technique and inject the celiac axis and/or the superior mesenteric artery in order to delineate the anatomy of the arteries of the liver.

This method is especially useful in determining anomalous arterial supply to the liver and neoplastic obstruction to the hepatic arteries, and thus helps to decide the proper placement of the catheter for later chemotherapeutic infusion.

Several common variations of the hepatic arteries are briefly described.—*John Allyn Tobin, M.D.*

MISCELLANEOUS

Karas, Joseph S., and Stanbury, John B. Fatal radiation syndrome from an accidental nuclear excursion. *New England J. Med.*, April 15, 1965, *272*, 755–761. (From: Rhode Island Hospital, Providence, R. I.)

The authors report a case of accidental nuclear exposure of a 38 year old man. He was pouring a "dirty" mixture containing U^{235} from a polyethylene cylinder 12.5 cm. in diameter and 120 cm. high into a tank 63 cm. in diameter containing sodium carbonate.

The patient recalled a flash of light and was hurled backward and stunned, but did not lose consciousness. He immediately ran from the building to an emergency shack 200 yards away, discarding his clothing as he ran. He complained of abdominal cramps and headache immediately; he vomited and had incontinence of diarrheal stool, which according to his colleagues was bloody. He was wrapped in warm blankets, taken to a nearby hospital and transferred at once to the Rhode Island Hospital. He arrived there 1 hour and 43 minutes after the accident.

The patient succumbed 49 hours after receiving 10–20 times a lethal dose of neutrons and gamma rays. It was estimated that there was a total whole-body dose of 8,800 rads.

The authors discuss the management of the victim of a nuclear accident in regard to radiation safety. The patient had heavy surface contamination of radiation-emitting isotopes. Furthermore, vomitus, sweat, urine and feces were all contaminated with radioactive sodium and P^{32}. Thus, there was the problem of radioexposure to the personnel caring for the patient, and of the disposal of contaminated clothing, linen and radioactive excreta. Finally, there were the additional problems of significant skin contamination during intimate care imposed by a patient who was for a time delirious and unmanageable, as these patients often are. Various laboratory studies on blood and excreta were also carried out, as well as radioactive scanning of the entire body and of the excreta.

The principal clinical problem was that of maintenance of blood pressure and the competence of the heart.

The article should be read in its entirety by anyone who is especially interested in nuclear accidents and radioactive contamination.—*C. Peter Truog, M.D.*

McCANDLESS, JAMES B. Accidental acute whole-body gamma irradiation of seven clinically well persons. *J.A.M.A.*, April 19, 1965, *192*, 185–188. (Address: Calle Post Esquina El Bosque, Box 1079, Mayagüez, Puerto Rico 00709.)

In July of 1962, 5 men and 2 women were accidentally exposed to whole-body irradiation from 4 to 100 r at the Puerto Rico Nuclear Center. Complete hematologic and bone marrow studies were done. Stool examinations, urinalysis, electrocardiograms, sperm counts, and daily complete blood cell counts were carried out. Special attention was paid to the skin, eyes, gastrointestinal system, water intake and output, and reproductive system.

Because this incident involved pure gamma irradiation, comparison of the hematologic findings with other accidental exposure cases involving neutrons in the same dose range has special importance in estimating the relative biologic effectiveness of fission neutrons on human leukocytes. Accurate dosimetry and a known energy spectrum (average 2 mev.) enhance the value of these findings.

Atypical lymphocytes were very common the first few days except in the patient who was exposed to only 4 r. Lymphocyte counts were unstable in the 4 patients who received the highest doses; lymphopenia and neutrophilia developed on the fourth to fifth days. In the proven absence of infection, toxicity, or trauma, it is probable that irradiation did cause hematologic abnormalities. Normal lymphocyte count and the absence of atypical lymphocytes are evidence of very low levels of acute exposure, less than 8 r in this instance.

It is important that a daily plot of neutrophils and lymphocytes be done on patients known or suspected of exposure to acute radiation dosage (greater than 20 r) to confirm the diagnostic value of this fourth to fifth day neutrophilia with leukopenia.—*Lois Cowan Collins, M.D.*

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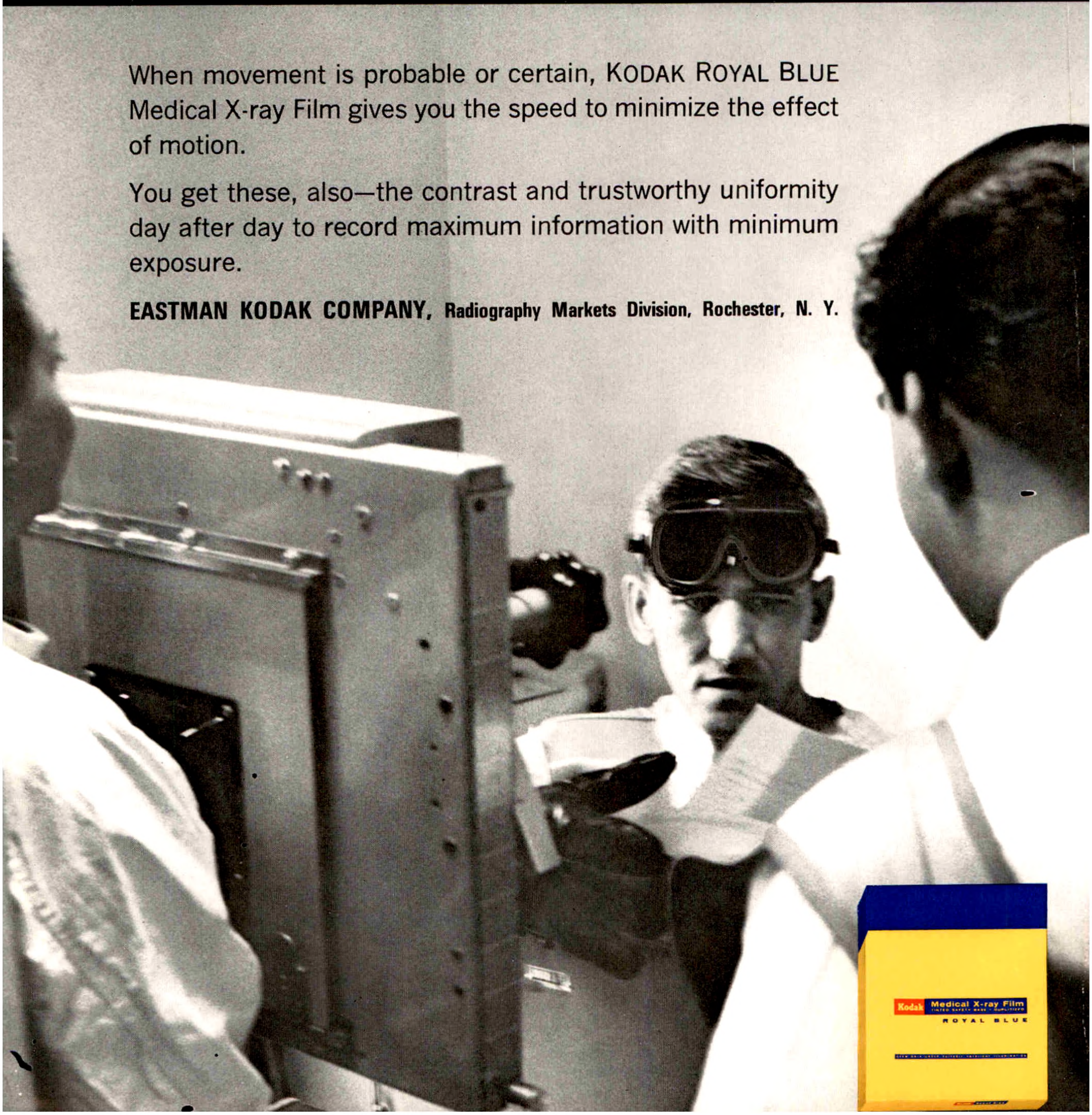

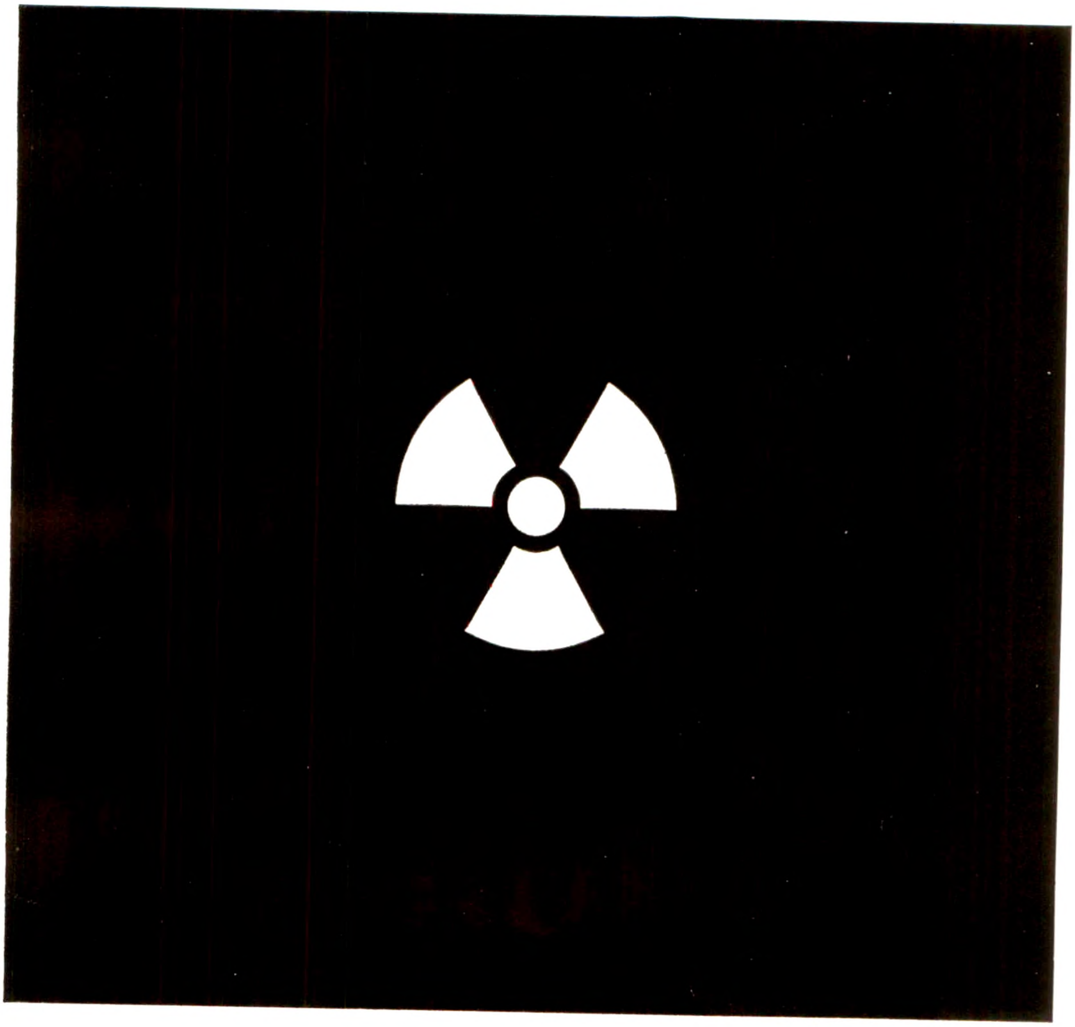

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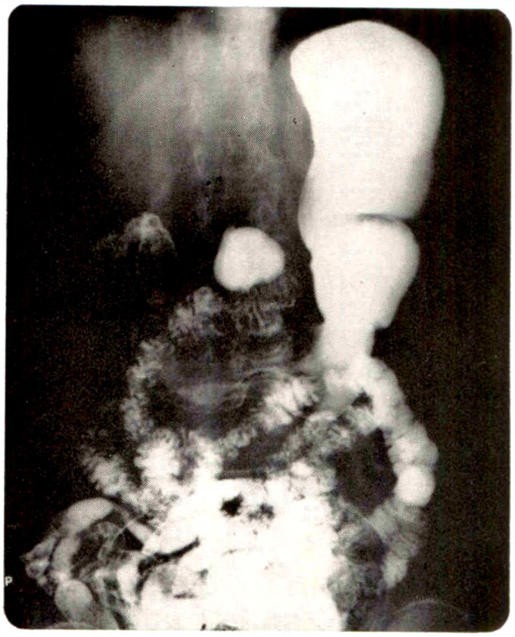

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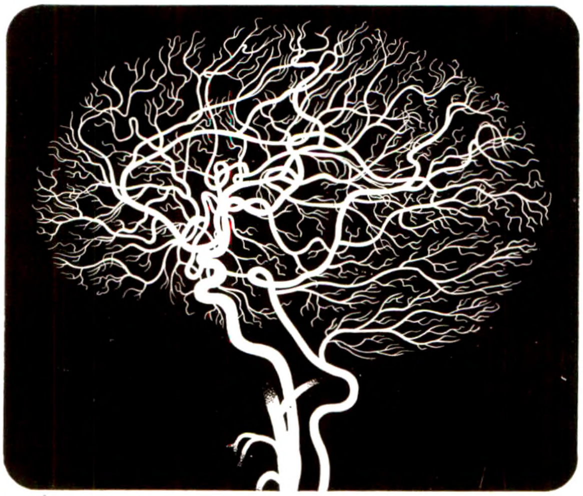

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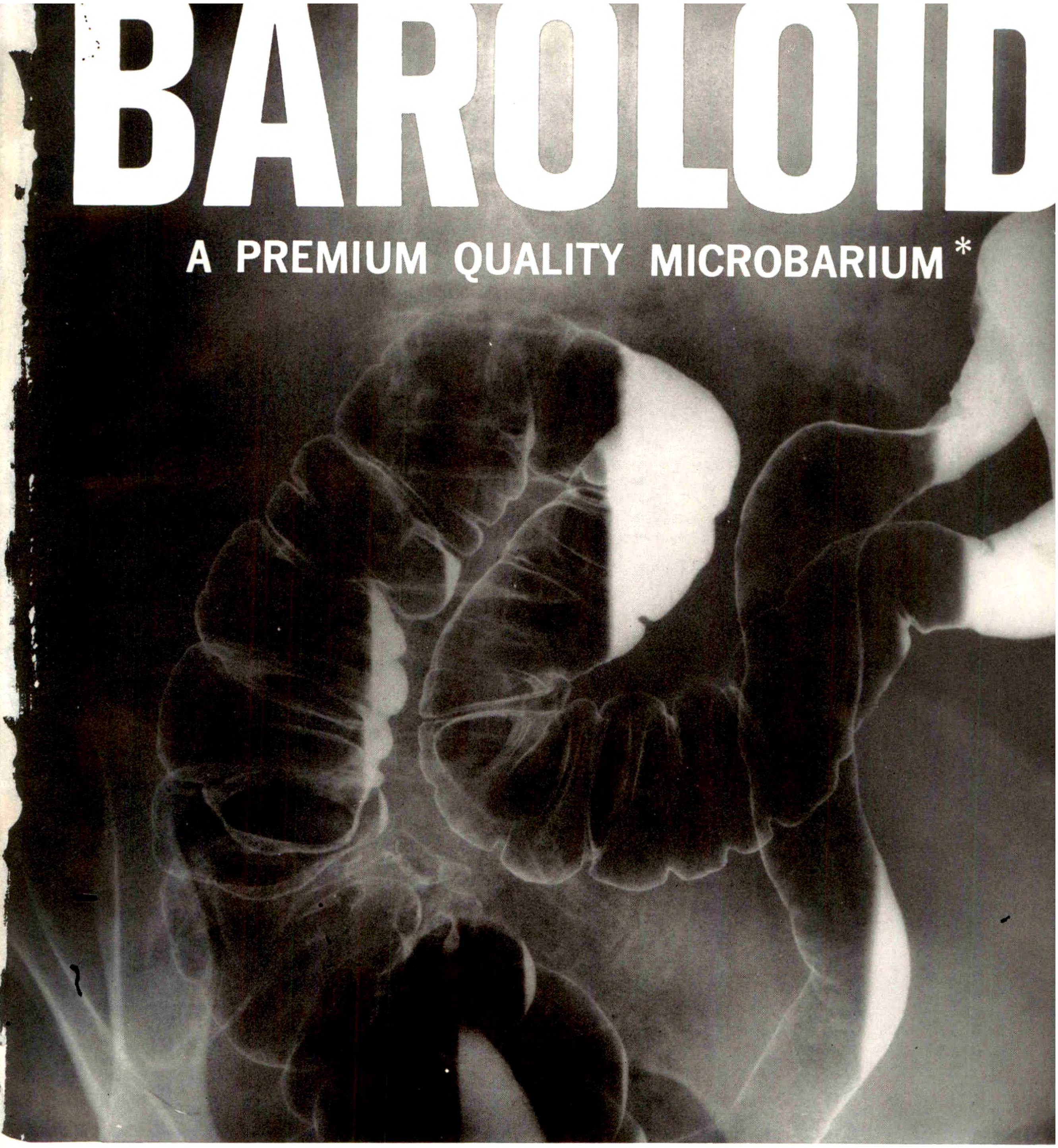

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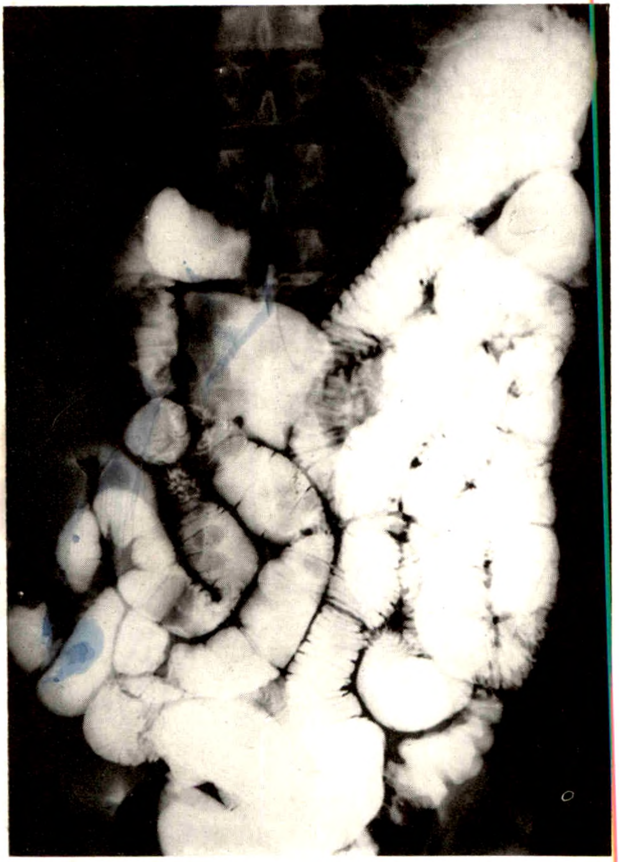

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